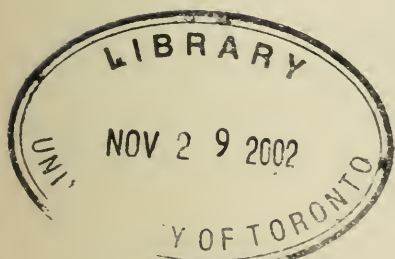


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to me that the method adopted was, thyrotomy apart, the only possible therapeutic resource.

Some may be inclined to call in question the diagnosis in this case, but a little consideration will, I think, convince any one that every other condition could be excluded.

Before concluding, I have to express my thanks to Dr Bankart for his valuable assistance both in recording some of the cases and more especially in superintending the execution of the corresponding drawings.

Meeting V.—February 15, 1893.

MR JOSEPH BELL, *President, in the Chair.*

DISCUSSION ON MYXŒDEMA.

1. THE CLINICAL FEATURES OF MYXŒDEMA.

By BYROM BRAMWELL, M.D., F.R.C.P. Ed., Assistant Physician to the Edinburgh Royal Infirmary; Lecturer on the Principles and Practice of Medicine, and on Practical Medicine and Medical Diagnosis, School of Medicine, Edinburgh.

IN introducing this part of the subject, Dr Byrom Bramwell said:—When, Sir, our Secretary was kind enough to ask me, in the name of the Council of the Society, to give a description of the clinical features of myxœdema, I had some hesitation in agreeing to the request, for I felt that I had little to say which was not already well known to the members of the Society, most of whom have doubtless had opportunities of seeing and studying the disease. And this leads me to say that a remarkable feature connected with myxœdema is its great frequency in this part of the country. I suppose there cannot be less than twenty-five or thirty cases of myxœdema and sporadic cretinism in Edinburgh at the present time.¹ I have at present four cases under my care in the Infirmary, and during the past two months I have seen other four cases in consultation in private practice. From a statement made to me recently by a medical friend in Dundee, it would appear that myxœdema is quite as prevalent in that city as in Edinburgh; and

¹ Dr John Thomson and I have both independently been struck by the fact that myxœdema and sporadic cretinism are especially prevalent in a particular district of Edinburgh. We are at present collecting facts with regard to this question, and will be greatly obliged if members of the Society who have had, or who now have, any cases of myxœdema or sporadic cretinism under observation will give us full details as to the residence of the patients, and especially as to the locality in which the patients were living—(1) at the time when the disease commenced, and (2) before the first symptoms were noticed.

the disease is comparatively common (probably quite as common as it is in Edinburgh) in the North of England.

It is difficult to account for this remarkable prevalence of the disease in this neighbourhood, unless by some endemic, telluric, or climatic condition; possibly the cold and damp (particularly the damp) of our climate predispose to the production of the disease. It seems necessary to suppose some such local predisposing or exciting cause; for otherwise it is exceedingly difficult to account for the fact that in some parts of the world the disease seems extremely rare, while it is, comparatively speaking, so common here. Professor Hoffmann of Berlin, who was recently in the Infirmary, and to whom I was showing a case of acromegaly and the cases of myxœdema which I have under treatment, told me that myxœdema is extremely rare in some parts of Germany. In Heidelberg, where he lives, he has only seen one case. At the same time he stated that within the past few years he had seen eight cases of acromegaly,—all, with one or two exceptions, collected from a radius of within twenty miles round Heidelberg. Now, acromegaly, which seems to have some relationship with myxœdema, is undoubtedly very rare in this country, although probably more common than is usually supposed. In some parts of America, too, myxœdema seems to be very rare. A gentleman who is present this evening—Dr Mackenzie of Cincinnati—tells me that he has never seen a case either in private or hospital practice, and he is physician to a hospital containing more than four hundred beds. Dr Mackenzie does not think that any case has ever been met with in Cincinnati.

The clinical features of myxœdema are now so well known and so very striking, that it is impossible to mistake the condition when it is fully developed. Different cases of the disease, as I have elsewhere pointed out, bear a very striking resemblance to one another. This was very well illustrated in a case which I have at present under treatment in the hospital. One day I took my son, a second year's medical student, into my ward and showed him this case of myxœdema. He had never been in a medical ward before. I had not, of course, told him anything about the case; further, he did not know that there was any case of myxœdema in the ward; and yet, when I put the case before him and asked him what it was, he at once recognised it by its resemblance to the plates in my *Atlas*. It is a very remarkable fact that a disease with such striking features and peculiarities has only been recognised as a distinct clinical entity since the year 1873. As I have elsewhere remarked, the disease must, however, have been known to many physicians before that date. When I entered practice in the year 1869, my father showed me a typical case of the disease, and pointed out its peculiarities to me.¹

¹ Since the discussion on myxœdema, I have learned from Dr Ireland of Prestonpans, that in the year 1854 he was called to attend the landlady of a

Myxœdema is essentially a disease of the middle and later life, and of middle-aged and old women, for it occurs much more frequently in women than in men. It is more common, too, in women who have borne large families than in the unmarried. But as everybody knows, it is by no means confined to females and to adults. It not unfrequently occurs in men as well as in women, and it may develop at any age. There is no doubt that the curious condition termed sporadic cretinism is the infantile form of myxœdema.

I may remark, in passing, that when myxœdema does occur in young women or young men the facial appearance of the patient is often not quite characteristic. The pink blush on the cheeks, which is such a very striking feature of the disease in older people, is often entirely absent.

In describing the clinical features of myxœdema it may, perhaps, be interesting to refer, as I go on, to two diseases which have some relationship with myxœdema,—namely, exophthalmic goitre and acromegaly,—and to detail the points of contrast and resemblance between them. As everybody knows, the thyroid gland is atrophied or absent in myxœdema and sporadic cretinism; whereas it is enlarged and hypertrophied in exophthalmic goitre. In acromegaly, on the other hand, the pituitary body is usually enlarged, while the thyroid gland is sometimes also affected; and it is very interesting to note that there seems to be some sort of complementary relationship between the thyroid and the pituitary, for one of the most important pathological facts which has recently been observed in connexion with myxœdema is the circumstance that in many, perhaps in all cases, the pituitary body is notably increased in size.

In the case which is represented in this Diagram, and which is one of the cases of myxœdema which I have recorded in my *Atlas*, the pituitary body was markedly increased in size. Through the kindness of Dr John Thomson I had the opportunity of making a post-mortem examination in this case some ten days ago. I shall not, however, detain you by referring either to the clinical or pathological features of that case, which is one of great interest, for Dr John Thomson intends, I believe, to lay a note of the condition before you at our meeting to-morrow.

Exophthalmic goitre, like myxœdema, is very much more common in women than in men; but it differs from myxœdema inasmuch as it very generally occurs in young women. Acromegaly, too, almost invariably develops in young adults. It seems equally common in the two sexes.

The onset of myxœdema is usually very slow and insidious. It

friend, a medical student in Edinburgh, who was suffering from the disease. On looking back to that case, which proved fatal a year after he first saw her, he distinctly remembers that all the striking peculiarities of the disease were well marked; when attending this patient he recognised that the disease was peculiar, and that it did not conform to any known form of dropsy.

is quite exceptional to find the symptoms developing rapidly; in those cases in which the disease appears to develop more rapidly than usual, it is highly probable, I think, that it has existed in an unrecognised form for some time previously.

An increased susceptibility to cold, inability to perspire, a feeling of lassitude and repugnance to exertion, both of body and mind, are, so far as my observation enables me to judge, usually the first symptoms of the disease.

As the condition goes on, a striking change takes place in the appearance of the patient; and when the disease is fully developed, the physiognomy is highly characteristic. There is an increase in bulk of the whole of the body,—the face, trunk, and limbs all being affected. This increase is due to a solid œdema, which does not pit on pressure like an ordinary dropsical swelling. The increased bulk of the body as a whole, and the swelling of the individual parts, are essentially due to this œdema,—to an enlargement of the soft parts rather than of the bones and joints. In this respect myxœdema contrasts in a remarkable way with acromegaly. In that disease the bones and cartilages, more particularly the bones of the extremities (hands, feet, nose, etc.), are enlarged, as well as the soft parts; for in acromegaly the soft tissues are also notably implicated.

I may say, in passing, that one of the most remarkable results which follows thyroid feeding, or the hypodermic injection of an extract of thyroid gland, in cases of myxœdema is loss of weight and bulk. One of the cases which I have had under treatment recently, and in which a complete cure, so far as the symptoms are concerned, has taken place, lost a stone and a half in a week or ten days.

In fully developed cases of myxœdema the face is full, coarse, bloated-looking, and round; it has been termed "moon-shaped." In this respect there is another striking difference between myxœdema and acromegaly. In both diseases the soft parts of the face may be full and swollen,—the nose and lips, for example, being markedly thickened and enlarged in both diseases; but in acromegaly the face is elongated and oval instead of round and moon-shaped.

The swelling of the lips is usually a striking feature of myxœdema. The lower lip especially is full, and feels firm, tense, and elastic. It resembles more or less closely in feel a piece of india-rubber. This elastic swelling very quickly subsides under treatment. In the course of a week or ten days I have seen the lower lip become quite soft and flaccid.

The nose is broad and coarse-looking. The eyelids are usually markedly affected. There is often a baggy, dropsical-looking swelling beneath the lower lid, which at first sight is suggestive of Bright's disease. The upper lid in many cases droops over the eyeball; and in order to prevent the loss of sight which is occasioned

by this drooping of the upper lid, there is often a compensatory elevation of the eyebrows, due to a permanent contraction of the occipito-frontalis muscle. The skin of the eyelids is usually soft, translucent, and waxy-looking.

As I have just stated, the appearance of the eyelids and the swollen condition of the face are highly suggestive of Bright's disease; and there is no doubt that, before the clinical features of myxœdema were known and recognised, cases of myxœdema were often put down as cases of kidney disease. But on closer scrutiny, the facial appearance is very different from that of kidney disease.

In typical cases of myxœdema a pink blush is present on each cheek. In some cases the blush is not confined to the cheek; in some cases, as in that which is represented in this Drawing, it involves the nose. The colour of the face, too, is usually different from that of Bright's disease. The skin has a yellow, tawny tinge, quite different from the pallor which is such a striking feature in those cases of Bright's disease in which the face is much swollen; while the baldness, or the thin, dry, harsh condition of the hair, the dirty brown encrustation of the scalp, and the thinness or absence of the eyebrows, which are such important characteristics of myxœdema, are absent in Bright's disease.

The tawny, yellow discoloration of the skin is chiefly seen on those parts of the body which are exposed to the atmosphere. This discoloration may persist after the œdema has completely disappeared under treatment. I hope to show you to-morrow a patient who has been cured by thyroid feeding. In her case the yellow discoloration of the face persists. It contrasts very remarkably with the whiteness of the scalp, and is seen to be limited to the parts of the skin exposed to the light; for the skin under the ears is quite white, while the adjacent skin of the neck and face is markedly yellow.

I have now referred to the more important changes which myxœdema produces in the face. The alterations which occur in the other parts of the body are no less striking and characteristic. The tongue is usually large and swollen; the buccal mucous membrane, the fauces, pharynx, and larynx are in many cases also œdematous. The swelling of the soft parts of the back of the mouth may be so considerable that the patient may experience considerable difficulty in swallowing. The hands are markedly enlarged and broad—"spade-like," as it has been termed. The feet present the same changes. The abdomen is usually full and large, and the trunk, as a whole, looks markedly increased in size. Puffy, elastic swellings, which are usually, it is said, the result of localized collections of fat, are sometimes seen at the root of the neck above the clavicles. In the patient whose case is beautifully represented in the water-colour Drawing which I shall now pass round, these supra-clavicular swellings were more marked than in any other case of adult myxœdema which has come under my own observa-

tion. In children affected with myxœdema (sporadic cretinism) the elastic subclavicular swellings are much more constant than in adults.

In patients affected with myxœdema and sporadic cretinism, although the neck is usually short, thick, and swollen, the rings of the trachea can usually be very distinctly felt, and in the great majority of cases no evidence of the thyroid can be detected during life. This is just what we would expect, for in the great majority of cases of the disease the gland is markedly atrophied, while in the juvenile form of the disease it may be altogether absent. In those exceptional cases in which the thyroid is present or enlarged the structure is altered and destroyed,—in other words, it is functionally inert.

Let me here say, in passing, that it is very difficult to determine by palpation during life whether the thyroid is actually present or not. This difficulty was well brought out in the post-mortem examination which I made in conjunction with Dr Thomson the other day; in that case, even after deflecting the skin of the neck, we were unable to feel the thyroid, but on further dissection we found that the gland was present. At the first glance it looked of normal size; its superficial extent was quite equal to that of a normal thyroid, but it was so soft and flabby, and so closely applied to each side of the trachea, that it was difficult to feel it; even after the skin had been deflected, it could not be differentiated by palpation from the trachea, with which it lay in close contact.

Such are the gross alterations and the more striking changes in the physiognomy which myxœdema produces in its advanced and fully developed stage.

When we come to study the condition more minutely we find evidence of profound alteration in the nutrition of the skin and its appendages, and in the functional activity of the nervous apparatus. The skin is dry, harsh, and rough. The total absence of sweating is a very striking feature in the great majority of cases. Flat moles are sometimes developed on the surface of the body. The hair becomes dry, harsh, and thin. In many cases the eyebrows are entirely wanting; in the advanced stages of the disease the scalp may be almost entirely bald, but whether this is so or not, it is usually covered with dirty brown crusts. This condition is, I think, one of the most striking features of the disease, and of great diagnostic importance. It is often possible to diagnose myxœdema merely by looking at the back of the neck and scalp. The thin, ragged, dry condition of the hair, the shrivelled, yellow, wrinkled appearance of the skin of the back of the neck, and the dirty brown scales or crusts on the scalp, have enabled me in several cases to recognise the disease before I had the opportunity of looking at the face. The nails often become dry and brittle, and the teeth not infrequently drop out or become carious.

I may say, in passing, that, under the influence of thyroid feeding, the production of sweating and of peeling of the skin are striking phenomena. I now pass round Photographs of a case which I hope to bring before your notice to-morrow, in which the peeling was quite as marked as after a severe case of scarlet fever. I have observed this peeling in several cases. Under the thyroid feeding the patient may be said to get a new skin; but I need not go into details with regard to this point now, although it is of very great importance.

The condition of the skin in myxœdema contrasts very remarkably with that which obtains in exophthalmic goitre and acromegaly. In exophthalmic goitre the skin is soft and moist. A tendency to excessive perspiration is one of the most striking features of exophthalmic goitre. In consequence of the dry condition, the electrical resistance of the skin in myxœdema is very much increased, whereas in exophthalmic goitre, in consequence of the soft, relaxed, and moist condition of the skin, the electrical substance is notably diminished. In acromegaly, too, the skin is usually soft and relaxed, and a tendency to perspiration is often a marked feature. In acromegaly a luxuriant growth of hair is usually a striking feature; whereas in myxœdema, as I have already pointed out, baldness is often very prominent. In acromegaly numerous fine pedunculated warts are apt to be developed on the surface of the skin; while in myxœdema, as I have just pointed out, flat moles are often present.

In myxœdema the expression is stolid, heavy-looking, and apathetic, and the facial appearance reflects the condition of the sensorium. One of the most striking features of the disease is the slowness with which cerebration, especially speech and muscular movements, are carried out. The gait is heavy and clumsy; I have termed it "hippopotamus-like." The speech is slow, thick, monotonous, and measured. These alterations in speech and movement, no doubt, depend partly upon the increased bulk of the body (in the case of the movements of the limbs), and on the swelling of the tongue, lips, larynx, and external organs of speech generally; partly upon the slowness with which the motor nerve apparatus functionates. The swelling of the tongue and fauces also accounts for the difficulty in swallowing to which I have previously referred. And I may say, in passing, that some patients complain of choking sensations, and not unfrequently they speak as if they had something in the mouth. All the cerebral actions of myxœdematous patients are apt to be carried out in a slow and deliberate manner. They often take a long time to answer a question; the "reaction time" is, no doubt, greatly prolonged.

This slowness of thought and action is very striking in many cases of sporadic cretinism. Children affected with sporadic cretinism will often sit for hours together perfectly quiet, apparently taking no notice of or interest in their surroundings; but

quite happy, comfortable, and contented so long as they are sitting in the sun or before a hot fire.

The stolidity of myxœdenatous patients compares very remarkably with the hyper-excitability of patients affected with exophthalmic goitre. Nervousness, tremor, and unrest are striking features of exophthalmic goitre; whereas stolidity and placidity are characteristic features of myxœdema.

In some cases of myxœdema, more profound mental alterations are developed. The mental deterioration is sometimes so great that the patient has to be sent to an asylum; although I am disposed to think that the cases in which definite mental alterations, either in the direction of depression (melancholia or dementia), or of excitement (delirium and mania), are developed, are much less frequent than the statistics of the Clinical Society would lead one to suppose.

Slowness of thought and mental deterioration are not, however, necessary features of myxœdema. In a well-marked case which I recently saw with Dr Menzies, and which has improved remarkably under thyroid feeding, the mental faculties of the patient were quite keen and acute. It is important to remember that, even when profound mental disturbances are developed, they are merely the result, in most cases at all events, of functional derangement of the nerve centres, and are not of organic disease. The remarkable way in which the mental symptoms may entirely clear off, in the course of a few days or weeks, under thyroid feeding, proves this. The fact, too, that the mental condition of patients affected with the infantile form of myxœdema (sporadic cretinism) may entirely change in the course of a few weeks is one of the most extraordinary features of this remarkable disease. I hope to show you to-morrow a little patient, $8\frac{1}{2}$ years of age (a typical case of sporadic cretinism, which I have recorded in my *Atlas*) in which the mental condition has become completely transformed in the course of five weeks as the result of thyroid feeding. I may say, too, that in that case the patient, who had only grown 2 inches in the previous two years, has grown no less than an inch during the five weeks that she has been under treatment.

The alterations on the sensory side of the nervous apparatus are less striking and important. Sight and hearing are sometimes, though comparatively rarely, impaired. The tactile sensibility of the skin is in some cases very distinctly diminished; but whether this is due to an alteration in the sensory nerve apparatus, or merely to the altered condition of the skin itself, is, I think, doubtful. Both conditions probably account for the alteration. The changes in the reflexes are not of any great importance, and need not detain us.

Hitherto I have been speaking of some of the more important alterations which can be observed by the physician himself. There are still some others to which I must refer. I must also say a

word or two with regard to the symptoms of which patients affected with myxœdema generally complain.

Debility and languor and increased susceptibility to cold are the most striking and important. The increased susceptibility to cold is highly characteristic. Myxœdematous patients are almost invariably worse in cold, and better in warm weather. And this increased susceptibility to cold is not merely a subjective symptom ; for the temperature in myxœdema is subnormal, and the temperature variations are much less marked than normal. The morning and evening temperature are often practically the same ; the diurnal rises and falls which occur in health may be almost entirely absent. I have noticed, too, that in many cases of myxœdema the temperature does not rise under conditions which would tend to elevate it in health.

In these respects myxœdema contrasts very remarkably with exophthalmic goitre. In that disease the patient often complains of subjective feelings of heat (flushings), and elevations of temperature not unfrequently occur. The temperature equilibrium, which in myxœdema is abnormally stable, is in exophthalmic goitre very easily disturbed ; trivial excitements and external irritations, which in health would produce little or no temperature disturbance, are apt to cause very considerable elevations in cases of exophthalmic goitre.

In acromegaly, as in myxœdema, the temperature may be subnormal. I do not know whether this is always the case or not ; but in the patient whose photograph I will show you presently, a subnormal temperature is a marked characteristic.

In myxœdema the pulse is usually less frequent than normal. Here, again, there is a very remarkable contrast with exophthalmic goitre, in which, as everybody knows, acceleration of the action of the heart is *the* most striking and constant feature of the disease. In acromegaly, as in myxœdema, the pulse may be slower than normal.

Some anæmia is usually present in myxœdema ; but the alterations in the blood do not present any notable peculiarities. Both the red blood-corpuscles and the hæmoglobin are usually moderately diminished in amount. In some cases of acromegaly, the same form of anæmia is also met with.

The condition of the internal organs in myxœdema does not call for any lengthened remarks. As I have already stated, myxœdema is most frequently developed in women who have borne large families ; and in many cases of myxœdema, amenorrhœa is present. In some cases this is perhaps the direct result of the disease ; but in others it is no doubt due to the fact that the myxœdematous symptoms only become freely developed at or after middle age—at a time when menstruation is about to cease. There can be no question, however, that there is a distinct

functional relationship between the thyroid gland and the sexual apparatus. It is well known that in some women the thyroid enlarges during the menstrual period or after sexual excitement. In one of the cases of myxœdema which I have been treating with thyroid feeding, menstruation, which for many months previously was arrested, has been restored with the cure of the disease; and this notwithstanding the fact that the patient is 48 years of age.

In another of the cases which is making rapid improvement under thyroid feeding, a still more curious phenomenon has been observed. The breasts have become hard, painful, and turgid—full of milk. On squeezing the breasts in this case, jets of rich milk could be easily propelled from the nipple.

The tendency to the production of amenorrhœa in myxœdema is another point of contrast with that which obtains in exophthalmic goitre. As already stated, exophthalmic goitre is most frequently developed in young unmarried females, and the menstruation in exophthalmic goitre is usually excessive.

Myxœdematous patients rarely become pregnant after the disease has fully developed. In many cases this is no doubt due to the fact that they are old; but this explanation only holds true in a certain number of cases. Young women affected with myxœdema do not usually become pregnant; and pregnancy, if it should develop, seems to exert a deteriorating effect on the disease to make it advance more rapidly; whereas it is well known that in exophthalmic goitre marriage and pregnancy often prove curative.

In acromegaly, like myxœdema, amenorrhœa is usually developed. In fact, in acromegaly amenorrhœa is a constant symptom. In many cases of acromegaly the first symptom is the sudden arrest of menstruation.

In many cases of myxœdema the urine is quite normal (although the amount of urea is usually diminished); in others a certain amount of albumen is present. In some cases the albumen is doubtless due to associated cirrhosis of the kidney. In old people affected with myxœdema, some cirrhosis of the kidney is often, of course, present. But in other cases the albumen appears to be the direct result of the myxœdematous condition itself; and that this is so, is shown by the fact that the albuminuria may completely disappear, in the course of a few weeks, as the result of thyroid feeding. This was the case in one of the patients whom I am at present treating in the hospital.

In old people affected with myxœdema, the arteries may be atheromatous and the heart degenerated. I may say, in passing, that this is a very important point in regard to treatment. Thyroid feeding is apt, as I shall explain to-morrow (I am anxious not to refer in any detail to the treatment to-day lest I should anticipate anything which Dr Lundie has to say) to produce very remarkable depression; in those cases in which there is reason to suspect any

disease or degeneration of the heart or arteries, the treatment has to be conducted with very great care, and the remedy has to be administered in very minute doses until the effect which it produces is accurately measured and watched.

The course of myxœdema is usually long and chronic. The more marked alterations which the absence of thyroid tissue seems to produce are functional in character. The disease does not kill, as a rule, until it has lasted for many years. That the changes are functional is clearly shown by the extraordinary rapidity with which they entirely disappear after a few weeks of thyroid feeding.

The *diagnosis* in typical and fully developed cases of myxœdema presents no difficulty. The clinical picture which these cases present is so striking, that when once one has seen a case it is impossible to help recognising it. It is only in the early stages and in imperfectly developed cases that a difficulty of diagnosis can occur. In young persons, as I have already remarked, the pink blush on the cheeks, which is such an important diagnostic feature, may be entirely absent. In the early stages, the swelling of the face, and the slowness of thought, speech, and movement, being often much less striking, are apt to pass unnoticed. In the earlier stages, increased susceptibility to cold, a subnormal temperature, dryness of the skin, absence of sweating, fulness of the face, especially of the lower lip, a feeling of lassitude and debility, and repugnance to active exertion, whether of body or mind, are the chief features of diagnostic importance.

The *prognosis* of myxœdema has entirely changed within the last few months. Before Dr Murray introduced his method of subcutaneous injection of thyroid extract, the prognosis was extremely bad. In some cases, no doubt, a certain amount of improvement occurred under friction, warm baths, diaphoretics, and tonics; but the disease was rightly looked upon as incurable, for these measures were merely palliative. They did not, and from the nature of the pathological change could not, be expected to produce any or real and substantial amelioration. Now, provided that there are no complications, and the patient is not too old, the prognosis is eminently hopeful. It may, I think, be safely stated that the symptoms of myxœdema may be entirely removed in the course of two or three months by the introduction into the body of thyroid extract, either in the form of subcutaneous injection, or better, through the stomach by thyroid feeding. I must not, however, say anything further on this, which is by far the most interesting and important part of the subject. I have avoided, so far as possible, alluding both to the pathology of the disease, and also to its treatment; but I hope at our meeting to-morrow to have the opportunity of bringing before your notice several cases of the disease which are at present under treatment, and of referring in more detail to the effects of thyroid feeding.

(In the course of his remarks Dr Bramwell passed round a series of water-colour Drawings, Photographs, and Temperature Charts ; and concluded by exhibiting on the screen a series of Photographs illustrating the clinical features of the disease.)

2. *Prof. Greenfield* read his paper on the PATHOLOGY AND MORBID ANATOMY OF MYXŒDEMA, which was illustrated by microscopic and lime-light demonstrations. His pathological connexion with the subject, he said, had been of long standing. It had been his good fortune, when pathologist at St Thomas's Hospital, to make the post-mortem on the case of Dr Ord's, which was the ground for his first report on the condition, and on which he founded the name *Myxœdema*. The primary most essential fact in the pathology of the disease was the atrophic change in the thyroid gland. There was little accurate knowledge as to the cause of this change. The functions of the thyroid gland were obscure, even with the light that modern investigation had thrown upon them. It was only certainly known that in some way this highly-vascular, ductless gland was concerned in the metabolic changes of the nutritive fluids, and that it had some relation to the elaboration of mucin. It probably secreted a material of the nature of a ferment, which rapidly passed into the blood and stimulated the secretion of the skin glands, and in some way acted upon the heart. In myxœdema the thyroid gland was atrophied, and in sporadic cretinism it might be almost entirely absent. In exophthalmic goitre there was an exactly opposite condition,—an enormous increase in the secreting structure of the thyroid, and also of the colloid material in the spaces of the gland. In ordinary cystic goitre, however, associated with cretinism, there was an enormous increase in its substance. Therefore we should not regard the morbid appearances of the thyroid in myxœdema as of too great importance, or put out of our minds other considerations in relation to its function. A very important control research would be to ascertain if feeding with thyroids produced any conditions in the system analogous to those in exophthalmic goitre. In myxœdema the sweat glands and sebaceous glands acted defectively, and later atrophied together with other parts of the skin. The normal transpiration being deficient, the lymph seemed to tend to accumulate and stagnate. That this was partly at least correct, seemed to be proved by the remarkable improvement often seen from the action of hot-air baths. There was one point which did not seem to have been observed, and that was the altered reaction of patients with myxœdema to tuberculosis. They seemed to show a marked proclivity to tuberculosis, while in its course and manifestations the tubercular process was largely modified. All the five cases of myxœdema from which he showed specimens died from phthisis, as well as a case of sporadic cretinism he had had. The tubercular processes were characterized by exceedingly rapid progress when they once set in. The power of repair in

myxedema was good, to judge from his experience of a case in which it was necessary to do a surgical operation. He had studied microscopically material from seven cases of myxedema and one of sporadic cretinism. In all the cases the thyroid was diminished in size. There was either generally or in parts an advanced condition of atrophy with fibrous overgrowth. In some all gland tissue had disappeared. In some the fibrous tissue was highly cellular. In one there was a lymphoid infiltration. These changes corresponded with what occurred in all glandular atrophies. The changes in the epithelium were also parallel to those seen in all wasting glands. Changes were found in the arteries similar to those found in all chronic interstitial inflammations. In the skin there were marked changes in all the glandular elements and in the hair follicles. They showed various stages of atrophy. Often there was an extensive deposit of pigment in the skin. The epidermis became very thin. The oedema appeared to him to owe its characters to the fact that it was more deeply situated than in ordinary anasarca. In the case of other parts, such as the lips and tongue, the oedematous condition was also quite deeply situated. In the tongue, patches were often most marked at a distance of a third of an inch or more from the surface. The change might be called a myxomatous degeneration of the tissue. In the skin, tongue, and other organs there were sometimes areas of dense fibrous overgrowth. The other organs in his cases, with the exception of the lungs, which were affected with tuberculosis, were in a practically normal condition. In the kidneys, however, there was occasionally a peculiar swelling and pallor, due to the presence of a myxomatous degeneration around the arteries at their division, and an extension of a myxomatous and cellular infiltration between the tubules in that position, while the cortex was normal. He had found no change in the nervous system, except in the peripheral nerves, in which there were frequently indications of a chronic neuritis. How far this change was due to the disease he was unable to say. The lymphatic glands and suprarenal capsules were normal. He concluded by showing a number of lime-light views illustrating the morbid changes in myxedema. Among these he showed a section of the thyroid gland of an old man who died of cirrhosis of the liver, which showed changes exactly resembling those found in myxedema.

3. THE TREATMENT OF MYXEDEMA.

By ROBERT ALEX. LUNDIE, M.A., M.B., B.Sc., F.R.C.S. Ed.

Two years ago the subject of my paper would have been easily disposed of; for myxedema had proved, so far, one of the most intractable of diseases. It must not be supposed that treatment had been altogether unavailing: a number of cases had been

benefited more or less. Protection against cold, persistent use of hot baths with vigorous friction did much good; among drugs, iron, strychnia, arsenic, nitro-glycerine, and especially jaborandi or pilocarpine, had all proved useful. The more favourable surroundings in hospital conferred temporary benefit on some cases, and a removal to a mild and genial climate on others. Still, little advance had been made since Dr Ord wrote,¹ "The progress of the disease is not readily affected by any remedy. The prognosis is altogether unfavourable."

Now, as I hope to show, there are but few diseases so certainly amenable to treatment.

While the therapeutic aspect of the disease was but little changed from its first description up to 1890, knowledge of its proximate cause had rapidly advanced. In Dr Ord's original paper² the atrophied condition of the thyroid was noted and figured. In 1882 M. Reverdin, and in 1883 Prof. Kocher, described a group of symptoms closely resembling myxœdema, which had followed in many cases total removal of the thyroid gland for goitre. In 1883 M. Reverdin commented on the resemblance of the two conditions; which was, however, in this country first called attention to independently by Dr Felix Semon. A committee of the Clinical Society of London undertook the investigation of the subject, and in connexion with its work Prof. Horsley began his remarkable experiments on animals which first satisfactorily established the fact that the cause of the symptoms of myxœdema is loss of function of the thyroid gland.

Prof. Schiff, von Eiselsberg, and others, proved that transplantation of a thyroid from another animal previous to thyroidectomy might diminish or prevent the subsequent degeneration. Horsley³ followed this up by suggesting transplantation of a thyroid from one of the lower animals as a treatment likely to be useful in myxœdema. Similar operations had already been performed on cases of "operative myxœdema" by Bircher in 1889, and by Kocher so far back as 1883.⁴ Horsley's suggestion was soon acted upon, and with at least temporary benefit in most cases. Relapse, however, usually took place; the longest persistence of improvement after a single operation I have found reported is in a case of Mr W. J. Collins,⁵ where the patient is said still to have felt well more than a year after transplantation. But the uncertainty and transiency of the effect of this operation was a bar to its general adoption.

One circumstance in connexion with transplantation attracted the special attention of those watching its effects, namely, that

¹ *Quain's Dictionary of Medicine*, article "Myxœdema."

² *London Medico-Chirurgical Transactions*, vol. lxi.

³ *British Medical Journal*, 1890, vol. i. p. 287.

⁴ *British Medical Journal*, 1890, vol. ii. p. 201.

⁵ *Medical Pioneer*, October 1892, p. 6.

improvement was perceptible the day after the operation,—much too soon, therefore, for the gland to have become vascularized and functionally active in its new situation; and it was suggested that this was due to absorption of the juice of the transplanted gland.

Dr G. R. Murray of Newcastle, reasoning on this observation, was led to try the effect of subcutaneous injection of an extract of sheep's thyroid, and obtained remarkable success. His results have been confirmed by numerous other observers. But the inconvenience and risks of the subcutaneous method led to several independent trials of the effect of internal administration, which proved equally satisfactory.

The first of these cases published in this country were those of Dr Mackenzie (33)¹ and Dr Fox (34), which appeared simultaneously last October. I had independently arrived at the same result; but the first to establish the success of this method seems undoubtedly to have been Prof. Howitz (40) of Copenhagen, who communicated his result to the Congress of Naturalists at Copenhagen in July last.²

My patient, an unmarried lady, then aged 54, had begun to suffer from increasing stoutness and inability to exert herself about fourteen years before I first saw her. Dr Campbell of Dundee, to whom I am indebted for some notes of her case, saw her a few years after her symptoms began, and finding the urine albuminous, suspected that she was suffering from chronic Bright's disease. But he soon came to the conclusion that her disease was myxœdema; and though she had more than one attack of congestive nephritis while under his care, she has now no albuminuria, and no sign of Bright's disease.

Her swelling and other symptoms fluctuated greatly; but every winter from 1886 to 1891 she had a severe exacerbation of some kind. The last, early in 1891, was characterized by persistent and distressing delusions.

When I first saw her in July 1891 I found her suffering from the characteristic symptoms of myxœdema in a very marked degree. The features were heavy and expressionless, the skin of the face much swollen and waxy-looking, with the characteristic flush on the cheeks; everywhere the skin was dry and harsh, the epidermis cracking and falling off in thick flakes. In the supra-clavicular regions, and to a slightly less degree over the parotid glands, there were prominent elastic swellings. The tongue was large and swollen; the soft palate so much thickened that it almost closed the pharynx. From this cause she had the rare and distressing accomplishment of being able to snore with her mouth shut. Her movements were slow and heavy, her walk was awkward, and she could not walk or stand for more than a moment or two without a

¹ The figures within parentheses refer to the numbers of cases in Table.

² *British Medical Journal*, 1893, vol. i. p. 266.

stick or other support. Her speech was slow, thick, and hesitating; and her mental faculties were similarly dulled. Naturally of a bright, lively disposition, she seemed oppressed by the weight, physical and mental, of her disease. And no one who saw the dull, heavy, clumsy aspect of face and figure, gait and gesture, could wonder that it was so.

Appetite, for some kinds of food, and digestion were good, but bowels sluggish. The heart's action was rather weak, but not otherwise abnormal; the radial pulse was quite difficult to feel through the thickened integuments. No thyroid gland could be detected. The temperature was generally about 95° in the mouth; the extremities were always cold. Menstruation still continued regular on the whole; but there had been an occasional intermission for a few months. She suffered from frequent, often almost constant, headache and giddiness, but they were rarely severe. She was almost always drowsy, even by day; at night she was often tortured by ghastly dreams.

Treatment by injection under the skin of the back was begun in October 1891,—but for the first month, as I afterwards discovered, with thymus instead of thyroid extract. During this time, except that some higher temperatures were observed (once $97^{\circ}8$), there was no improvement.

On November 28th the first real thyroid extract (Brady & Martin's) was given, representing two-thirds of a sheep's thyroid; and this was repeated five times at intervals of a week. After the second injection the patient began to experience improvement; after the third there was a very striking diminution of the swelling in face, tongue, palate, and hands; and in the succeeding weeks this process went on at a startling rate. It reminded me of nothing so much as the fairy tales, where magic potions make the body grow large and small at will.

She lives with a twin sister, whom she used to resemble so closely that they were constantly being mistaken for each other. When I first saw them I found it difficult to believe they were sisters at all. But when the swelling diminished it was very curious to see the counterpart of the sister's face being gradually revealed as the mask of myxœdema melted away.

The diminution in swelling was attended at first by an increased feeling of well-being, and a sensation of lightness and activity to which the patient had long been a stranger. But very soon this was qualified by the onset of pains, first in the lower part of the face, neck, and chest; a little later in the back and arms, and for a short time in the scalp. These pains were generally aggravated after exertion, and when at their worst were very intense. They were accompanied by great tenderness in the painful parts on slight pressure, so that their seat appeared to be the skin or subcutaneous tissue. Moreover, after the fifth injection the appetite failed, and for several days there was much nausea, with a feeling of weakness.

At this time, too, the drowsiness, of which she had complained much before, was replaced by insomnia.

After a month's interval another injection (representing one-third sheep's thyroid) was given (January 22nd, 1892). Just about this time an inflammatory swelling developed at the lower part of the vagina, which led to an abscess, and continued to discharge and to give some discomfort for several months.

Injections (representing one-third sheep's thyroid) were given again regularly every week from February 12th; but the fifth of these caused a considerable abscess, and after April 1st they were discontinued. There had been no local reaction to speak of before; that is to say, till suppuration had occurred spontaneously at a point far away from the injections. About five weeks later the patient began to feel her old symptoms returning, and the deterioration quickly showed itself in slowing of the speech, as well as visible increase of the swelling.

On June 4th, therefore, the injections were resumed with redoubled antiseptic precautions; but two out of three caused abscesses, so that I was forced to abandon them. Even these three had, however, produced some improvement; and about this period perspiration was observed, the first time for many years. On July 9th I gave two very small injections in the forearm, but even these caused considerable inflammatory thickening, though not abscesses.

Under such circumstances it was clearly impossible to go on administering subcutaneous injections, yet the patient was most anxious that the treatment should be continued. I began, therefore, on July 16th to administer the extract by the mouth,—I must say with small hope of success. It was immediately evident, however, that the physiological effect could be obtained in this way as satisfactorily as by injection; and the patient has continued the treatment ever since, and has remained in very much better health than previously, though her condition has not been quite so good during the winter as it was in the autumn and latter part of the summer.

The photographs taken at the commencement of treatment (October 1891) and a year later respectively show better than a long description could do the improvement in her appearance. The face is natural, and has a bright, intelligent expression; everywhere the swelling has much diminished, and the skin is soft and pliant; speech is vigorous and quick; she can stand and walk easily without a stick or other support, and can assist in household duties which were before impossible for her; the pulse is readily felt; the temperature usually 97° or more,— 98° on the last two occasions when it has been taken; the extremities warm and comfortable.

She kindly wrote down for me her own impressions of the result of treatment; and though it involves a little repetition, I need

make no apology for quoting her description, written on 25th January 1893:—

“During last year my health improved immensely. From sitting weakly and drowsily in my chair (and almost invariably in pain), I have become lively, strong, and active, with good appetite for many forms of food which before I could not touch, and am able to enjoy life. I am considerably decreased in bulk, and my arms and hands so strengthened as to enable me to carry with ease what before I could scarcely lift. I can sew heavy work, when formerly I could not hold the needle.

“In the summer months I perspired freely (though not all over), which I had not done for very many years. For years I had suffered from confused headache, sometimes severe, but in the early part of January 1892 it left me entirely; and although I am not quite so well now (cold weather affecting me), I am still able to go about and make myself useful in various ways.”

I have encountered one very curious difficulty in maintaining the treatment, which deserves to be farther considered. Pains precisely similar to those I described as following the first series of injections continue to trouble her whenever the dose of the thyroid extract is increased beyond a certain point. They have never been so severe as on the first occasion; but they are sufficient to limit her activity, and cause her sometimes considerable inconvenience. They are usually accompanied by breathlessness, which, like the pain, is readily induced by exertion. She herself professes to recognise a distinct difference between this and the form of breathlessness with which she used to be familiar as one of the myxœdematous symptoms.

So much are these symptoms associated with the taking of the extract, that she herself says, when the dose is reduced to a point at which the pains are absent, that “she feels as if the medicine were not doing her any good;” and, in fact, on one occasion there was distinct evidence of relapse when this condition was maintained for some weeks. At present she is taking extract corresponding to $\frac{1}{15}$ th sheep’s thyroid daily, and this seems as much as she can stand.

With regard to the cause of the pains, and the other unpleasant symptoms met with, it seems profitless to speculate till we know the effect of similar doses on healthy individuals.

Ever since I began using thyroid extract I have avoided all other methods of treatment, with the single exception that I have from time to time found it necessary to resort to the administration of cardiac tonics. There is no reason why most of the methods that had previously done good in myxœdema should not be used concurrently with the thyroid treatment, except that it seems, in most cases, not to require to be supplemented.

During the last eighteen months more than forty cases of myxœdema treated either by subcutaneous or internal administra-

tion of thyroid gland or its extract have been noticed in the medical journals. The first and most striking fact about them is that amelioration of the symptoms has almost invariably been effected. In only two (10, 11) where the result is stated is there said to have been no improvement; and as those two are reported by the same observer, I think it may safely be assumed that there was some error, probably in the method of procedure. Excluding these cases, then, we may say that treatment with thyroid gland *invariably* does good to cases of myxœdema,—a statement that could be made with regard to very few of our therapeutic procedures in any disease.

But if it always does good to the symptoms of myxœdema, it certainly cannot be said that it never does harm to the patient. The catalogue of more or less unpleasant results is somewhat formidable. A few have been associated only with subcutaneous injections. Abscesses, as might be expected, are of not infrequent occurrence (1, 9, 22, etc.). Dr Murray¹ has met with "flushing, nausea, and stabbing pain in the lumbar region. Once there was also loss of consciousness, and general tonic muscular spasm for a few seconds." And Dr Hearn (12) reports that on one occasion "the skin became so livid as to be almost blue-black; then followed tremors, quivering of the limbs, and complete unconsciousness, which lasted about a quarter of an hour."

But besides these results, which seem directly dependent on the method of administration, there are others due to later physiological effects, as they have also occurred after administration by the mouth. These may, in the main, be classified under the heads of—1, Weakness; 2, Pain; 3, Nausea: all these have been mentioned in the account of my own case.

1. *Weakness*.—One of Dr Hale's patients (27) said "that she, to a great extent, lost the use of her hands for two days" after an injection; and again, had "weakness and pain in the arms following the injection for some hours." Another (28) had "frequent fainting-fits" after one injection; and after another "felt 'queer,' and unable to raise her arms."

Dr Fox's patient (34), under larger doses than were meant to be taken, "noticed she was getting rapidly weaker, profuse perspirations breaking out on the least exertion; she was unable to walk or stand steadily." Dr Holman's patient (37) suffered from "tumultuous action of the heart at night," with very rapid pulse.

2. *Pain*.—One of Dr Hale's cases (27) suffered from "much giddiness and headache for twenty-four hours." In Professor Bouchard's cases (19, 20), "headache and pains in the chest and limbs" compelled the treatment to be suspended.

Dr Mackenzie's patient (33) "complained of aching pains all over;" while Dr Cresswell Baber's (36) had "sharp headache and

¹ *British Medical Journal*, vol. ii. 1892, p. 449.

intense aching in the back and limbs, which continued for three days, and obliged him to keep his bed."

3. *Nausea*.—Dr Beadles' patient (25) said "that she always felt hot, and had a sense of sickness after the injections." One of Dr Hale's patients (28), already referred to, "after the first few injections was troubled for some hours with sensations of faintness and nausea."

Dr Mackenzie's (33) and Dr Baber's (36) patients had nausea, and the former vomiting as well as pain.

None of the *contretemps* above noticed, though some of them must have been very startling, seems to have led to any serious result. But two of Dr Murray's patients (5, 6) died suddenly, apparently from cardiac failure, after having undergone treatment by injections. Both were feeble and over 60; and, especially in the absence of information as to the post-mortem appearances, the connexion of the fatal result with the treatment must remain doubtful.

My own patient seems very nearly to have met a similar fate. On June 17, 1892, having had an injection a few hours before, she drove into the country, and after arriving at her destination exerted herself much more than she had done for some time. She was suddenly seized by a feeling of extreme faintness and breathlessness, and became livid. She was laid down, had a stimulant administered, and very soon recovered; but from the description that was given me of her condition, I believe her to have been for the time in very great peril. In this case, as in Dr Murray's, I do not think it can be regarded as by any means certain that the thyroid extract caused the attack of faintness; but it must be looked upon, at all events, as under suspicion.

In connexion with these occurrences, however, a remark made by Dr Woodhead last year¹ is of very great importance. He said, "That in a series of experiments in which he had injected various extracts of different glands into rabbits, he was particularly struck by the effect on the heart, as very frequently degeneration of the muscle tissue ensued." It seems most important, in view of the future use of the thyroid treatment, that careful experiments should be undertaken with the view of determining the precise conditions of this occurrence, and particularly whether internal administration of gland extracts has the same effect as injections.

Meantime, patients must be carefully warned of the risk of unusual exertion, at all events in the earlier stages of the treatment.

I have spent so much time on the consideration of these toxic effects because I wish to bring out clearly the great and unexpected activity of the remedy with which we have to do. I think they may, in the great majority of cases at least, be avoided by using moderate doses and judicious methods of administration.

With regard to the effects of similar administration of thyroid

¹ *British Medical Journal*, 1892, vol. ii. p. 452.

in health or in other diseases than myxœdema and its allies, I have been able to gain hardly any information, except that it has been tried by more than one physician with entirely negative results in exophthalmic goitre.

The cases already put on record are sufficient abundantly to prove that thyroid gland or its extract can relieve, and in some cases practically cure, myxœdema. Of course it would be unreasonable to expect it to take effect upon all the results and complications of a severe case of the disease; but the recorded effects in some cases have gone far beyond the most sanguine of reasonable expectations; and when more than one case with insanity (9, 25) and one with severe nephritis (37) have been found to improve greatly in these respects as well as with regard to the strictly myxœdematous symptoms, I think it would be rash at present to assign limits to the possibilities in this direction.

Deterioration is generally evident after a suspension of the treatment for a few weeks: it is natural to expect that continuous treatment will be required to counteract a continuously acting cause of disease. Experience only can show whether the improvement attained at first can be maintained indefinitely. It seems likely, however, that an agent capable of ameliorating the disease, even in an aggravated form, will be able to keep it permanently in check if steadily persevered with. To remove the cause is at present beyond our power, and, except in the earliest stages of the disease, will probably always remain so; unless, indeed, farther experience points out a means of securing a certain and permanent result by transplantation. The present thyroid treatment cures myxœdema, not in the sense in which scabies or ringworm, ague or syphilis, is cured, but in a very real and practical sense,—that in which constipation is cured by the continuous administration of purgatives. The morbid tendency is not removed, but artificially counteracted.

The thyroid of the sheep has generally been used; but cows', calves', and pigs' thyroids have also been tried, apparently with equally good results. Care must, of course, be taken to secure, as far as possible, healthy glands. Dr Napier¹ states that he has found more than 50 per cent. of sheep's thyroids to "show more or less evident indications of deviation from normal structure." But the sheep, being comparatively little liable to tuberculosis, seems to be the most satisfactory animal available from which to obtain the remedy.

The doses given have varied enormously, from $\frac{1}{120}$ th of a thyroid hypodermically (31) to two thyroids daily by the mouth (33, 40). The former is probably too small; the latter very speedily proved far too large a dose. But it is no wonder, considering the indifference, not to say contempt, with which we have been accustomed to regard the thyroid, that heroic doses should have been tried.

¹ *Lancet*, 1893, vol. i. p. 273.

In one case (21) doses of one-sixth gland subcutaneously were followed by pain and weakness; most effects of that kind have not been produced except by larger doses.

One-fourth to one-half gland weekly, if administered subcutaneously, or one-half to one gland given by the mouth, seems to have been sufficient to bring about rapid improvement at the beginning of the treatment; and considerably less doses prevent a relapse when a condition approaching the normal has been reached. Perhaps it may be found more satisfactory to give smaller doses than I have mentioned from the first, and to be content with a less speedy result than has generally been aimed at; as in Mendel's case (31), where slow but distinct improvement resulted from hypodermic injections first of about $\frac{1}{120}$ th, later of $\frac{1}{80}$ th gland daily.

If we gave our patients their weekly allowance of digitalis or atropia, or any active drug—nay, may we not say their weekly ration of any ordinary food?—in a single dose, toxic symptoms would certainly be a pretty frequent result. Now, this is just what has often been done with the thyroid gland hitherto, and from this most of the unpleasant effects seem to have resulted. Now that it is proved that the gland is a very powerful remedy, such methods should be avoided in future so far as possible, and this can be done much more readily by internal than by hypodermic administration.

For this reason, as well as on account of obvious inconveniences, and the special risks of the hypodermic method already considered, I think treatment by the mouth is greatly to be preferred. It is said that the unpleasant effects immediately following hypodermic injections can be avoided by very slow administration. But even the mere possibility of producing an epileptiform convulsion is too serious a matter to be lightly regarded. The results of internal administration have been just as successful as those of injection; and I have seen no reason for preferring the latter. It is possible that stomachs may be met with intolerant of the remedy even in small doses; in that case rectal administration might be resorted to.

The form in which the remedy is given seems meantime not of essential importance. The raw gland, the liquid extracts prepared by various chemists, the solid extracts used by Dr Arthur Davies¹ and Dr Vermehren,² appear to be all equally efficacious. The raw gland, or a home-made extract prepared from it, has the advantage of cheapness; an extract manufactured on a larger scale will probably be of more uniform strength, and admit of more accurate dosage,—a matter of some importance, considering the activity of the remedy. If the extracts in powder prove stable, I think there can be no doubt that they will be found the most convenient and satisfactory. The method of partially cooking the gland introduces an unnecessary element of uncertainty of dosage, if, as seems

¹ *British Medical Journal*, 1893, vol. i. p. 289.

² *Semaine Méd.*, 8 Fév. 1893, p. 59.

probable, the physiological effect is destroyed by heat, and is therefore undesirable.

A number of interesting questions are opened up by this new departure, and some of them will probably soon be answered. For example—What is the nature of the active principle? What is its effect on healthy individuals? What is the cause of the pain and other unpleasant results encountered in the treatment? What other diseases (if any) are amenable to analogous methods?

Meantime clinical medicine and experimental physiology, working hand in hand, have achieved a result of which both may well be proud; a result which proves, if proof is needed, the value of patient and painstaking labour in fields apparently the most barren and unpromising; a result which *should* vindicate, once for all, even in the eyes of those most prejudiced, the importance to suffering humanity of that most maligned of men, the vivisector.

Dr Affleck moved that the discussion be adjourned.

The Adjourned Meeting was held on Thursday, 16th February, at 4.30 P.M.,—Mr Joseph Bell, President, in the chair.

Dr Affleck resumed the discussion on Myxœdema, and said that so many cases of myxœdema had of late appeared in the medical papers that it was quite evident that for a long time the disease must have been overlooked. Cases had been passed by as Bright's disease without albuminuria, or perhaps there was a trace of albumin suggestive of that condition. He showed two photographs of a patient with myxœdema whom he had seen several years ago, the one showing her as she appeared when first seen by him, and the other taken after she had undergone a course of the treatment then in vogue—namely, hot baths, friction, arsenic, and good feeding. The patient had certainly greatly improved. The temperature of this patient had never risen to the normal line the whole time she was under observation except once, when she took a severe feverish cold, which would have probably raised the temperature of an ordinary person to 104° . He had had several cases since, in all of which the temperature was habitually subnormal, and with little or no fluctuation. He thought we were as yet only collecting information about the whole subject, and on that account it was important that all who had cases should communicate them, in order that they might get as much knowledge as possible to bear on the subject. They should inquire into the antecedents of the patients, with a view to finding out the etiology of the disease. In most of his cases he had obtained a history of antecedent depressing influences, such as worry, anxiety, and hardship. There might, after all, he thought, be some nervous condition underlying the disease, which interfered with the

innervation of the thyroid gland and caused it to atrophy. It had been remarked that patients with myxœdema frequently became insane. He had had a case in which the converse occurred—in which an insane patient became myxœdematous. The patient was a woman of 48, who took cerebral hæmorrhage with left hemiplegia, and afterwards became melancholic and suicidal. Three years afterwards, when patient had somewhat improved, she became myxœdematous. Some very striking contrasts had been brought out by Dr Bramwell and Professor Greenfield between myxœdema and exophthalmic goitre. He thought that in Addison's disease they had another condition which presented an interesting analogy to myxœdema. He suggested that the effect of treating cases of Addison's disease with suprarenal capsules should be tried. There were also other diseases in which they might try analogous treatment. There was overwhelming testimony of the value of the treatment of myxœdema by thyroid feeding, and he welcomed it as a most important contribution to modern therapeutics. He then showed a boy who had been admitted to his ward a year ago with sporadic cretinism. Another member of the family suffered from the same disease. The patient had six toes on one foot, and two other members of the family had a similar deformity. He had treated the case by thyroid implantation, and not by thyroid feeding. Mr Caird had engrafted thyroid material into the mammary regions and tunica vaginalis. The patient had immensely improved, and the result, he thought, was a very remarkable one.

Dr John Thomson showed two cases of sporadic cretinism, both of which were under treatment with thyroid gland. They were both patients of Dr W. H. Miller. The first was a girl of five years. Patient seemed to be quite healthy until between two and three years old, when it was noticed that she was not growing as she should do, and was not so bright as she might be. When examined, seven and a half weeks ago, she was 32 inches in height. Temperature was subnormal. Skin was rough and scaly; hair coarse and scanty. She had a characteristic squat figure, and her hands also were characteristic. There was a tendency to coldness of the extremities, and there was puffiness of the eyelids. There were distinct supraclavicular swellings. Fontanelle was still open. The mental characteristics were those of all cretins. On the 24th of December last he began to give her thyroid gland by the mouth. She at first had one-eighth, and afterwards one-fourth of a gland (half of a lobe) twice a week. After three and a half weeks it was seen that she was very much better, and she had since gone on steadily improving. The face was less puffy and of a better colour, the skin softer and more moist. Temperature was now normal. The swellings in the neck had gone. Bowels were regular. She was much more intelligent. Her hair had grown very much, and the scalp, which had had a tendency to seborrhœa and eczema, had become almost quite

healthy. She had grown almost an inch in the time she had been under treatment.

The second patient, A. C., was a lad of 18 years and 8 months; seen first on December 17th, 1892, with Dr W. H. Miller, whom I have to thank for permission to observe and record the case, and for most kind co-operation in its treatment.

Family History.—His parents are strong, healthy, well-grown people, and temperate in every way; they were not related to one another. All his four grandparents lived to old age. No relative on either side has suffered, so far as is known, from myxœdema or sporadic cretinism. A maternal uncle had, in his youth, an illness which temporarily affected his mind; but with this exception there has been no case of nervous or mental disease in the family, and there is no history of phthisis.

The mother has had seven other children, one of whom died in infancy from pneumonia; the others are alive and very healthy in every way. She has also had two miscarriages. The patient is the fourth child, and ten years intervened between his birth and that of the third; during that time there was a miscarriage (about the third or fourth month) for which no cause was known.

Pregnancy.—At the time of the child's birth the parents were living in a northern district of Edinburgh, close to the Water of Leith. During pregnancy the mother had no accident or fright, and she felt very well, but she noticed that the child moved less than usual. There was nothing wrong with either parent at the time of the commencement of pregnancy.

Birth.—The birth was slow, but not difficult: the child did not breathe for some time after. At birth the child appeared of the usual size and normal in every way.

Past History.—He was given the breast for ten months, and he seemed to his parents to be quite like other children till he was between eighteen and twenty-four months old. His teeth were not late of appearing. The mother did not notice if the fontanelle was late of closing. He was not much later than other children in noticing things, or in talking. He was rather late of walking, but could walk by himself when he was about two years old.

Before the end of his second year his parents noticed that he was not growing; but it was only when he was about four years old that they became anxious about this. Not until he was about six did they realize thoroughly that he was more than merely backward in development.

During the last fourteen years he has grown little, if at all, in height, although he has got broader and stouter. His mental condition has gone back during that time, so that he is said to be much less intelligent than he was at five years old.

When about eight years old, he used to have frequent attacks of epistaxis on slight provocation (*e.g.*, on crying). At these times

he sometimes lost a good deal of blood, and he seemed brighter after them.

For many years (at least eight) he has suffered from a cough and wheezing, especially during winter.

State on Examination.—The patient is $33\frac{1}{2}$ in. in height in his stockings, and presents (see Plate I.) the typical ungainly appearance of a sporadic cretin.

The measurements of the head are as follows:—Circumference, $20\frac{1}{8}$ in.; from meatus to meatus, $12\frac{1}{2}$ in.; from root of nose to occipital protuberance, $13\frac{1}{2}$ in.

The fontanelles are closed. The hair is of a dark reddish-brown colour, and is coarse and scanty. The complexion is that characteristic of myxœdema—pale, yellowish, and waxy-looking. The eyelids are swollen and puffy. The nose is thick and somewhat turned up. The lips big, thick, and pale, and on the upper one there is an ulcer, due to constant picking; the ears are well formed.

The teeth are all of the temporary set, the second dentition not having begun. The incisors and canines and the left anterior molar are yellow and much ground down, but otherwise normal. The other seven molars are more or less carious, and several are only represented by stumps. The mucous membrane of the gums and throat is pale and coarse, but otherwise normal. The tongue is big, although it does not protrude unnaturally; it is fissured, and has large papillæ.

The neck is very thick, so that it appears short, and on each side of it there is a large flat fatty tumour in the posterior triangle. There are smaller swellings of a similar nature in front of each axilla, but none on the back of the chest. The rings of the trachea can be felt pretty distinctly, and nothing can be made out in the position of the thyroid.

The thorax seems natural in shape, and the heart is normal. Some thickening at the costo-chondroid junctions. There are numerous rhonchi heard all over the chest.

The abdomen is rounded and prominent, and there is a small umbilical hernia. The liver and spleen are not enlarged, and nothing abnormal is felt on palpation. There is slight dorso-lumbar lordosis.

The limbs are short and thick, the hands and feet broad and comparatively large. There is a slight amount of bowing outwards of the leg bones.

The skin, all over the body, is dry, harsh, and scaly. This is especially so on the legs, where large flakes are constantly coming off on to his clothes. There is considerable swelling of the subcutaneous tissue everywhere. There is no hair on the face, pubes, or axillæ. There are very numerous small moles in various situations, and a few flat warts.

The genital organs are small and infantile in form. The prepuce

is long and tight. There is no difficulty in micturition. The urine was not specially examined.

The temperature is always considerably subnormal. The patient is very chilly, keeping away from the door in cold weather, and liking to sit close to the fire.

Nervous System.—The cutaneous sensibility to all impressions is dull. The sight and hearing seem perfect; the taste and smell are also good, but probably not very acute.

All the organic reflexes are normal. Bowels very regular. Micturition is normal; but sometimes, especially if he is cold, he goes very long without making water (even fifteen hours), apparently forgetting to do so. If he goes too long he is apt to wet himself. The knee-jerks are well marked.

Mental Condition.—His intelligence is in most respects like that of a child of less than three years old. He can go little messages into the next room. He can repeat by heart one or two verses of hymns. He can name the numbers up to ten, but often misses one, and he does not seem able to count objects. He cannot say the alphabet, but knows some of the letters by sight.

His voice and laugh are very peculiar—loud, harsh, cracked, and unchildlike. His enunciation is indistinct and curiously deliberate. When he is in a happy frame of mind he can use a good many words; but sometimes it is difficult to make out what he wants, and he cries with vexation apparently when unable to express himself. With strangers he is extremely shy of speaking, even when quite friendly.

He is very fond of music, and sings a good deal in a sort of a way; when joining with others he can sing the tune correctly.

He notices a good deal more than one would think from his very stupid expression, and he gave, *e.g.*, to his father a tolerably intelligent account of his being clinically examined for the first time by palpation, percussion, etc.

He is generally tolerably happy, especially if taken notice of and played with; but if he is left to himself he sits apart and gets dull and torpid, not appearing to notice things or people. He often amuses himself with a bat and ball. He is somewhat irritable if teased, and shows his annoyance by crying out. He is not demonstrative in his affection, but he knows very well those who are kind to him, and shows marked preference accordingly. He has a doll to which he is much attached. He is also especially fond of the cat, and, indeed, of all animals; and he always wants to stroke them, and seems to have no fear.

His memory is pretty good. He recognised at once a sister who had been absent for five years.

He is very particular about having everything neat and tidy, and about the cleanliness of his clothes and person.

He sleeps heavily and very long—usually 12 to 15 hours; and

his mother says that he would sleep all day sometimes if he were left alone. He is especially drowsy in cold weather.

His muscles, although prominent and hard, are very weak, like those of a young child. He cannot grasp an object very firmly, and is very easily knocked over. His gait is peculiar and waddling.

Treatment.—He was ordered a quarter of a sheep's thyroid by the mouth twice a week. [By mistake he was twice (December 20th and 23rd) given a double dose (half a thyroid).]

Progress.—On *January 1st* (after two halves and two quarters) he began to suffer from headache and pains in the belly, back, and feet, and from sleeplessness and restlessness at night. The pains only began about 11 P.M., and seemed pretty severe. They lasted all night, but did not trouble him during the day. His appetite failed him entirely, and he stayed mostly in bed.

January 11 (after two halves and five quarters).—The headache and other pains are no better. His appetite has improved. He has suffered twice from hiccough, which he never had in his life before. His limbs seem to be a little tender, and he cries when his mother puts his arms back in dressing him. He says his hands are sore, and he slaps them to make them better. His face and body are distinctly less swollen than they were. To have an eighth of a thyroid twice a week.

January 14.—Pulse 140, weak and soft; respirations 32; temperature (in axilla), 98°·8. The swelling is getting rapidly less, and the skin is very much softer than it was; but as the patient is still restless at nights, and evidently feels ill, the thyroid treatment is to be stopped.

January 24.—The headache has ceased, and for three nights he has slept well. Pulse 110; temperature (in axilla), 98°·5. He has greatly improved in appearance, and his demeanour and complexion are much more childlike than they were. The supra-clavicular and other fatty swellings have disappeared. His mother says that he pronounces his words more distinctly, and that he is much more cheerful than she *ever* saw him before. Appetite good. Ordered to resume taking one-eighth of a thyroid twice a week.

February 16.—Shown at the meeting of the Edinburgh Medico-Chirurgical Society.

February 25.—During last month he has rapidly improved in almost every way. His temperature keeps normal (98°·2–98°·4). He has grown *two inches in height*, measuring now 35½ inches. His skin has quite changed its character, being almost as soft as that of a healthy child. Mentally, his parents say, he is distinctly brighter. He is, however, much thinner, and seems weaker than he was; and his bronchitis is worse. This last is due to his constantly running to the outer door, which formerly he used to shun because of his sensitiveness to cold. As it appears that his present



PLATE I.



A. C., aged 18 years and 8 months, at beginning of thyroid treatment, Dec. 25th, 1892.

PLATE II.



A. C., aged 18 years and 11 months, after three months of thyroid treatment, March 22nd, 1893.

rate of growth is probably of itself a source of danger, he is now to take only one-sixteenth of a gland twice a week.

March 22.—He has been exceedingly bright and well since last note (with the exception of an attack of diarrhœa, brought on by eating too much toffee). His appearance has wonderfully improved (see Plate II.). During the last three weeks he has not grown at all in height. This apparent arrest in the rapid growth formerly observed may be partly due to the smaller dose now taken, but seems mainly owing to the fact that the bones of his lower limbs are bending very considerably from too much standing and running about. Recommended to try cod-liver oil.

April 1.—Improving steadily, but cannot take cod-liver oil in any form because it makes him very sick. He has been kept off his feet a good deal, and has grown a quarter of an inch since last note. The two lower anterior molars are being pushed right out, apparently by the approach of the second set of teeth.

April 12.—General improvement continues, but he has caught a little cold, and his bronchitis is worse. He now measures fully 36 in. His hair is softer, more plentiful, and of a darker, less red tinge than before treatment. He now seems to have no inclination to sleep longer than the other members of the family.

Remarks.—Although the therapeutic interest in this case is, let us hope, little more than beginning, it seems desirable to publish it now, in order to draw attention to the marvellous benefit which we may expect from thyroid treatment, even in advanced cases of sporadic cretinism.

A comparison of the Plates shows, even more strikingly than the notes do, the radical change which the patient has undergone.

In Plate I., in spite of his infantile proportions, there is a look of premature maturity (if one may say so) about his figure, and even in his attitude there is a suggestion of decrepitude.

In Plate II., his whole aspect is changed. The dull apathetic glance is gone, he “eyes the world now like a child,” and even in the way he stands and grasps the stick he is holding there is something of vigour and hopeful vitality, so that one can hardly resist the conviction that (like a child) he has a long process of bodily and mental growth and development in front of him.

Ordinary nineteenth century therapeutics yield us no analogy to guide us in our conjecture as to how long the improvement so vigorously begun is likely to continue, or how far it is likely to go. Only time can show. But when we note the change in his appearance and character wrought in the short space of three months, we are certainly tempted to rather a sanguine prognosis.

Dr Byrom Bramwell showed a woman who was admitted into his ward in the Infirmary at the end of October last, suffering from myxœdema of five years' duration in a typical form. On the 8th

of November he commenced to give her half of a sheep's thyroid every day. In a few days the temperature went up to 100°, the pulse rose from about 45 to 80, and the patient became extremely prostrate. The tongue became foul and the breath offensive, and she had vomiting and diarrhœa. Pain occurred in various parts of her body, but it was felt most in the position of the thyroid. The treatment had to be suspended for a time. The marked derangement and depression produced in this case was, he said, a lesson to him to give very much smaller doses in the subsequent cases he had to treat. He was satisfied that large doses, especially in old people with atheromatous arteries, were not unattended with risk; for anything like the amount of depression which was produced in the case which had just been brought forward might very easily prove fatal in old or debilitated persons. In such cases probably one-sixteenth of a gland daily was sufficient. Treatment was resumed after ten days with one-quarter of a gland every three or four days. She was now practically cured. The whole skin had peeled in a very extraordinary way. She now perspired naturally, her temperature was normal, and her pulse was faster. She was bright and active mentally, and felt perfectly well. The scalp was smooth and normal, but the skin of the face was still markedly pigmented. She had done nothing for the last five years, but now felt so well that she was going to take a situation in a few days. He next showed a young woman who had been suffering from severe general psoriasis since May last. The remarkable peeling of the skin, indicating a profound alteration in its nutrition, seen in the former case, had suggested to him that thyroid feeding might be advantageous in psoriasis, and perhaps also in ichthyosis and some forms of eczema. He had therefore resolved to try the effect of the treatment upon this case. It had been commenced ten days ago, half a lobe being given every day. It had not produced much reaction, but it had had a most extraordinary effect upon the disease. The inflammatory condition had completely subsided, and the patches of psoriasis had begun to peel off in large scales, leaving a sound and healthy skin beneath. He also showed a woman, 33 years of age, who was admitted to the Infirmary on the 26th of December last, and who had been suffering from myxœdema in a typical form for three years, the disease commencing after the birth of her last child. The pink blush usually seen on the cheeks was absent. She had been treated first with one-eighth of a thyroid (one quarter of a lobe) daily, and afterwards with one quarter, and later with one-half of a thyroid daily, as the treatment was well borne. Latterly she had complained of marked pain in various parts of the body, palpitation, and a feeling of great debility and anorexia. She had no severe gastro-intestinal disturbance. The dose was reduced, and the unpleasant symptoms disappeared. The case was now in a fair way to cure. She was

resuming her normal condition. According to her friends, she now looked ten or fifteen years younger. An eczema which she had had on the back of her hand had disappeared. He also showed the case of sporadic cretinism which he had described on the previous day. In answer to a question, he said that he gave the gland chopped uncooked in rice paper. It would, he thought, probably be better to give a fixed dose in the form of a definite extract.

Dr William Russell showed a woman, aged 60, who showed all the symptoms of myxœdema in a very marked degree. No distinct history of the case was obtainable, but it was probable that the patient had suffered from the disease for twenty years. She weighed over 22 stones. Treatment had not yet been commenced.

Dr John Thomson also showed, for *Prof. Grainger Stewart*, a well-marked case of myxœdema in a woman 38 years of age, who had been ill for eighteen years. She had just come to the Infirmary for thyroid treatment.

Dr Alexander Bruce showed a case of myxœdema under the care of *Prof. Fraser* in the Royal Infirmary, which was being treated by thyroid feeding. Thirty grains, by weight, of the thyroid were given during the first month twice a week. Patient showed distinct improvement within a week of the commencement of the treatment. Pulse and respirations had increased in rate. The temperature had risen to normal. Her weight, which was 12 stones 10 lbs. when treatment was commenced, was now 10 stones 12 lbs. Her memory and speech had improved very much. Within three weeks of the commencement of the treatment she was able to knit. The only discomfort after the feedings had been headache or occasional pains in the limbs. One untoward feature that had developed, however, was a condition of relative anæmia. Patient had no murmurs when admitted, but now had basal and mitral systolic bruits. Blood-corpuscles had fallen from 4,600,000 to 3,700,000, and hæmoglobin from 78 per cent. to 59 per cent. An increase in the amount of urine and urea was noted. Otherwise her progress had been satisfactory. *Dr Chalmers* of St Ninians, who had recommended this case to *Prof. Fraser*, had another case under treatment in the country, and he had found that if thyroids were not given quite fresh they were apparently inert, and did no good.

Dr Russell showed numerous specimens of sheep's thyroids.

Dr Melville Dunlop gave an account of the following cases of myxœdema which he had lately treated:—

MR PRESIDENT AND GENTLEMEN,—I propose bringing under the notice of the Society the following six cases of myxœdema which I have had under treatment lately, partly because I think that they serve to emphasize the treatment of the disease by means of the thyroid extract, a *résumé* of which was last night so very ably and graphically brought before us by *Dr Lundie*, and partly because

my cases present some unique points, which, I venture to hope, may not be without interest for the members of the Society.

The first case to which I should like to direct the Society's attention is that of a single lady, aged 46, who has suffered from myxœdema for the last five years.

Her family history is specially interesting. Her twin sister has had exceedingly well-marked myxœdemic symptoms for the last twelve years, and she was, I believe, one of the first cases of the disease recognised in Edinburgh.

These ladies were patients of the late Dr Struthers of Leith, and their cases are well known to several members of the Society, who had an opportunity of seeing them in consultation with Dr Struthers. The following is an extract from a letter written by their mother in 1849, three years after their birth, she herself being at that time about 40 years of age:—

"I am getting very old-like, and have much difficulty in getting about. My colour is very bad, and I am exceedingly stout without being strong. I am assuming the corpulent look of advancing years, to my great dismay."

A bust of this lady, the cast for which was taken after death, bears many of the characteristic features of myxœdema, especially noticeable in the thickened lips and the swelling under the eyes.

Her nephew, now a well-known Scottish Academician, says, that from his remembrance of his aunt he has not the least doubt that she suffered from myxœdema, and other relatives bear him out in this opinion.

Further, my patients have been frequently told since the commencement of their illness that they were becoming like their mother, a likeness never previously remarked upon.

I have not the slightest hesitation in saying that another sister who died seventeen years ago, and whom I remember well, was a very typical and far-advanced case of myxœdema.

Her case was regarded as a very obscure one by the medical man who attended her.

I need not relate in any detail the symptoms of Case No. I., which were well marked.

The onset was very gradual, and the increase in bulk manifested itself slowly. She had gained about 4 inches round the waist, and she was about 2 stones heavier than she was before her illness commenced. She suffered greatly from stiffness and cramps in her muscles, and had much difficulty in rising from a chair, turning in bed, or in attempting to walk. Her tongue and soft palate were much enlarged, and the speech slow and deliberate. The temperature was 96°·6, and the patient was very sensitive to cold, and she was irritable and unhappy.

Treatment was commenced on October 8th, 20 drops of Brady & Martin's thyroid extract being given by the mouth, before

breakfast, three times a week. The patient was warned against making any special exertion, or exciting herself in any way, and was recommended to remain in bed on the days upon which the dose was administered. In ten days the temperature had risen to normal, and the patient felt comfortably warm, and did not wish to sit over the fire as formerly. Speech was much less deliberate, and the drawn, weary feeling about the forehead had gone.

October 28.—Lips moving much more freely, especially the under lip, and the patient is speaking fluently and naturally again. Her skin is softer and more flexible, and she feels less languid, and her spirits are markedly improved. The muscles of the arms and legs have lost the hard boardy feel, and all her friends notice a most striking improvement in patient's appearance. She moves about more actively, and with less of the air of "une grande duchesse." She no longer complains of the crampy pains in her limbs.

November 8, a month after the commencement of treatment.—The improvement is most striking. Patient's clothing, instead of fitting tightly, is hanging loosely upon her, and she has lost 10 pounds in weight. The face, instead of being square, is again assuming an oval shape, and the puffy appearance in the lower eyelids has quite vanished. Patient complains of aching pains in the limbs and over the neck and chest. A pair of gloves which she could not get on two months ago now slip on quite readily.

November 20.—Can again play on the piano, and can write, knit, and sew with ease. The tongue is greatly reduced in size. Patient does not become worn-out and exhausted nearly so readily as formerly. The heart's action has become very irregular and intermittent, and the patient complains of palpitation.

Accordingly the dose was reduced to 20 drops twice weekly, cardiac tonics were administered, and she was confined to bed for a few days.

December 2.—Palpitation and irregularity of heart's action greatly improved. Patient appears to be getting rather thin, and has had for the second time to tighten all her garments. Dose further reduced to 15 drops twice a week.

December 16.—General appearance, speech, colour, and temperament as they were before the commencement of the illness.

January 10.—Patient says that she feels quite well again, and perfectly cured. All her old aches and pains have disappeared, and she has regained her former activity, and walked a long distance without feeling tired. She still complains of some stiffness in the muscles on opening and shutting her hands. The tongue appears of a normal size again, and her hair is growing naturally once more, and has lost the dry scaly appearance, and the nails, instead of being brittle and hard, are quite smooth and polished. In the centre of each nail there is a prominent nodule, marking the date of the commencement of treatment, the upper or old half being cracked and brittle, and the lower or new half quite smooth and

natural in appearance. The dose was further reduced to 15 drops once a week.

January 18.—The patient has lost over 2 stones in weight, and the following comparison shows the difference in the measurements now and three months ago :—

	18th October 1892.	18th January 1893.
Abdomen, . . .	34 inches.	31 inches.
Waist, . . .	29 "	27 "
Calf, . . .	12½ "	11 "
Upper arm, . .	9½ "	9 "
Forearm, . . .	9¼ "	8¼ "

Patient continues to feel quite well, and can now go about as before her illness, and takes a keen interest once more in all that is going on. Dose reduced to 15 drops once a fortnight.

February 1.—The patient has experienced no bad effects from the reduction of the dose, and continues to feel quite well.

Remarks.—There was never any nausea produced by the thyroid feeding in this case, and the only symptom causing any inconvenience was the irregular and intermittent action of the heart, caused doubtless by the disturbance in the balance of the circulation, and which was quickly overcome by reducing the dose and confining the patient to bed for a few days, and giving a cardiac tonic. There was at no time any excessive perspiration produced; but the patient informs me that previous to her illness she does not remember perspiring even when she indulged in violent exercise.

The next patient, namely, the twin sister of the last recorded case, shows a still more remarkable result produced by the thyroid feeding. In her case the disease had lasted over twelve years, and there was an enormous increase in the size of the body as a whole, as well as of the individual parts. This lady had been completely invalided, and unable to move about or use her hands or arms for the last seven or eight years. The very least exertion caused her to lie back exhausted, and frequently induced attacks of syncope. She suffered much from cramp and pains in the muscles of the back and limbs. The usual signs of myxœdema were in this case well marked: her complexion, expression, speech, and the condition of the hair and nails were very characteristic. The skin was very dry and scaly, and there were large numbers of small warts covering the neck, and there was also much brown discoloration of the skin of the chest, back, and sides, occurring in patches. The temperament was most placid, and she had accepted her illness very philosophically. Conversation caused her much effort, and she often forgot words and names, and wandered from one subject to another.

During the few months preceding treatment the condition of

this patient had become much worse, both mentally and physically, and she had been altogether confined to bed. Gradually she became quite childish, and had hallucinations of sight, smell, and hearing. She continually declared that there were people in the next house trying to annoy her by speaking along electric wires connected with her bedroom. She imagined that *séances* of the Maskelyne and Cook variety were being conducted in her room. She saw people whispering, and complained that dogs and cats, cocks and hens, were annoying her with their peculiar sounds. The mental symptoms gradually became worse, and the patient became sleepless and restless, and refused food. By degrees acute mania developed, the patient throwing articles about the room, continually calling out loudly, and having a very wild and anxious expression. The tongue was thickly coated, and the restlessness and excitement were often so severe that it required considerable strength to restrain the patient, whose own strength was marvellous, considering her previous weak condition.

She had been in this state for over six weeks, under the care of mental nurses, when I determined to give the thyroid extract a trial, with, I must confess, but faint hopes of success.

The treatment was commenced on the 18th of October, 20 drops of the thyroid extract being administered thrice weekly. By the 30th of October the excitement had quite gone, and the patient was resting and sleeping quietly. She had no longer any hallucinations, and was speaking rationally, and she was again taking nourishment freely, but was very weak.

November 12.—Feels as if she were recovering from a long illness. She remembers that she had been in a very peculiar and excitable state. Temperature 98°·8 F. Patient is speaking much more freely, and face is already smaller and more mobile. She feels warmer and more comfortable, and no longer objects to the touch of a cold hand, as formerly. She perspires slightly every night, and the bowels now move regularly without the necessity of having recourse to aperients. The dose was reduced to 20 drops twice a week.

November 24.—Complains of rather severe aching pains in limbs and over the upper part of chest and neck. Voice is much stronger, and patient speaks naturally and quickly again. She cannot understand the reason for the change in her condition, the patient not having been informed that she was being subjected to any treatment, which was now explained to her.

December 7.—The skin is quite soft and satiny, and no longer harsh and scaly. Muscles have lost their hard and board-like feel. Pulse can again be felt, which it was quite impossible to do at the commencement of treatment, owing to the subcutaneous œdema. To-day patient sang one of the old English ballads from commencement to end without any effort, this being the first time she has attempted to sing since the commencement of her illness.

December 28.—The body is nearly half the former size, and the face is much smaller. The complexion is clear and natural, and the brown discoloured patches on the chest and abdomen are no longer visible. Patient no longer snores during sleep, and is perspiring freely. Hair is again growing thickly on a bald spot which has existed for many years, and a fresh crop of young hair is growing thickly all over the scalp.

January 14.—Patient is now able to be out of bed, and to sit up eight or nine hours daily, and is once more able to knit and sew. The thyroid extract is now being given only every alternate week.

The following are the measurements taken on the 18th October and on the 14th January:—

	18th October.	14th January.
Abdomen,	38 inches.	34 inches.
Waist, .	33 "	28 "
Calf, .	14½ "	11 "
Upper arm,	11½ "	10 "
Forearm,	10½ "	9 "

February 1.—Patient continues to improve, and feels like her old self. Many of her friends scarcely recognise her, so marked is the improvement in her appearance. The temperature has remained at normal since ten days after the commencement of treatment. She talks a great deal, and very quickly. Patient has experienced no bad results from having had no thyroid extract last week. She goes out in a bath-chair every day, and is feeling much stronger.

February 13.—Weight is now 10 st. 9 lbs., whereas three months ago it was 14 st. 10 lbs. Patient can sew quite dexterously again, and feels very happy at the change which has taken place in her condition.

CASE III. is that of a married woman, aged 43, whom Dr Haultain kindly sent to me for treatment. The disease had first manifested itself three years ago. She had been treated two years previously to the commencement of her illness for a large goitre, which had interfered with her swallowing, and which had gradually disappeared under treatment, until no trace of the thyroid gland could be discovered, and atrophy of the gland had supervened. The cure of the goitre had resulted in myxœdema, the cure in this case being worse than the disease. There was a great amount of solid œdema of the body, face, and limbs. Her complexion was very typical, being almost purple at the point of the nose and in the centre of the cheeks, and gradually faded into a pinky, and then into a waxy hue. The tongue was very large, the speech slow, the skin dry and scaly, the hair scanty and lustreless, and the lips were greatly thickened, and moved slowly and de-

liberately. Her hearing was greatly impaired, and was gradually getting worse, and she complained of buzzing sounds in both ears. Her temperament had undergone a great change, and instead of having a bright and happy disposition, she had become morbid and suspicious, was subject to delusions, and under the impression that some one was mesmerising her. The urine was scanty and acid in reaction. The heart sounds were feeble. The temperature was $96^{\circ}4$. Treatment was commenced on the 18th of November, 20 drops of the thyroid extract being administered thrice weekly.

December 1.—Temperature has already risen to normal, and the patient feels comfortably warm, and no longer desires to sit over the fire. Her mind is much clearer, and she feels as if a great weight has been lifted off.

December 10.—Hearing is greatly improved, and the sounds and buzzing in the ears no longer annoy her. Her friends are much gratified at the improvement in her appearance and speech, of both of which she is conscious herself. She perspires naturally.

December 20.—The choky feeling of which she used to complain has gone, and she can now swallow with ease. The very marked purple colour of her cheeks is quickly disappearing, and the complexion is assuming a natural colour. Patient feels much happier, and no longer regards her friends with suspicion. She is again able to sew, and has made a frock for one of her children, which she had not attempted to do for some years. Dose reduced to 20 drops twice a week.

December 28.—The puffiness about the eyelids is no longer visible, and the skin is much softer. Her mind is again clear and active, and all her friends remark upon the change in her appearance and spirits.

January 8.—Patient can again attend to her household duties and go about as of old, and last week walked a couple of miles without feeling fatigued. Dose reduced to 20 drops once a week. Patient says that she feels quite well again. Speech, complexion, and expression are perfectly natural, and no trace of the disease is left. Her hearing is now as acute as ever. She is much thinner, and has had to tighten all her garments, and she has experienced no bad effects from the reduction of the dose. Bowels now move daily. Dr Haultain, who had not seen her since the treatment was commenced, was much struck with the change in her appearance and temperament. Temperature remains normal. Measurements:—

	18th November.	1st February.
Abdomen,	. 41 inches.	35 inches.
Waist, .	. 33 "	28 "
Calf, .	. $14\frac{3}{4}$ "	$11\frac{1}{2}$ "
Upper arm,	. $11\frac{1}{2}$ "	10 "
Forearm,	. 10 "	9 "

February 14.—Patient continues quite well.

This case is a good example of the rapidity with which improvement takes place, all the symptoms having yielded to treatment in a couple of months.

My fourth case is that of a married lady, aged 56, in whom symptoms of myxœdema manifested themselves nine years ago. The disease developed very slowly, the patient gradually becoming stout and getting easily wearied. The complexion became bad and the eyelids swollen. The trunk and limbs were greatly infiltrated with solid œdema, and so greatly were the eyelids swollen, that, in order to see out of her eyes, she had to hold the eyelids apart with her fingers. The tongue and soft palate were much swollen, and she had difficulty in swallowing, and frequently choked. The face was stolid, square-shaped, and broadened out, especially in the lower half. The upper eyelids were much elongated and the eyebrows arched. The complexion was very characteristic of the disease, and the skin dry and scaly. Patient was very susceptible to cold, and always felt better in warm weather. Temperature 97°·2. She perspires slightly, and there is considerable increase in the secretions from the nose and eyes. Speech is slow and deliberate, and there is great muscular weakness, and the patient cannot walk any distance, and staggers when attempting to do so. Urine is very acid, sp. gr. 1010, and only about 20 ounces are passed per diem. Pulse is difficult to feel, owing to the thickening of the tissues. Appetite very good. Bowels are constipated, and the patient suffers almost constantly from piles.

December 31.—Treatment was commenced by giving 20 drops of the thyroid extract thrice weekly.

January 7.—Has been perspiring very freely,—so freely, indeed, that the night-dress has to be changed twice in twenty-four hours. Temperature has already reached the normal, and patient feels much warmer. Bowels are moving daily.

January 14.—Continues to perspire very freely. The thyroid is given before breakfast, and the patient commences to perspire about 2 o'clock, and continues doing so till the following afternoon. The perspiration has a thick, oily feel. Patient already feels much lighter and better, and has lost over 7 lbs. in weight in a fortnight.

February 2.—Patient has changed greatly in appearance, and is a stone lighter, being now 12 stones instead of 12 stones 13 lbs. Speech is much faster and tongue smaller. Patient no longer snores when asleep. She complains of aching pains over chest and limbs. Her friends are delighted at the change in her appearance.

February 12.—Has no longer to hold the eyelids apart when looking at anything. Œdema is rapidly disappearing, and perspiration is not so profuse. The saliva is much increased in

quantity, and runs out on the pillows. There is also a considerable discharge of mucus from the mouth and nostrils. Pulse can now be readily felt. Patient feels a great improvement in her condition, but is suffering from weakness, owing to the rapid loss of tissue. The improvement is so marked that a friend who saw her four weeks ago failed to recognise her.

CASE V.—Mrs R., aged 48, married. Illness commenced about twenty years ago, when patient found herself getting stout and losing strength. Her friends passed her in the street, failing to recognise her. The disease advanced very gradually, and during its course there have been periods of remission, during which the patient has felt better, and the swelling of the tissues has diminished. These periods have always taken place during summer.

Present Condition.—The body, face, legs, hands, and arms are all greatly swollen, and the legs especially have a hard, board-like feel. There is likewise a very great increase of hard, resistant oedema at the back of the neck. The hands are broad and spade-like, and the tongue is much enlarged. The patient notices that the swelling is always more marked in the evening. Temperature $96^{\circ}8$. Speech is slow and deliberate, and she suffers much from muscular weakness. The saliva is increased in amount, and the pillow is always wet in the morning. The usual symptoms of myxœdema are well marked. Treatment commenced on 21st January, 20 drops of the thyroid extract being administered thrice weekly.

January 24.—Patient feels nauseated and unhappy, and disinclined for food. Bowels somewhat relaxed.

January 28.—Temperature, 99° . Patient is perspiring about the chest and upper part of the body. She still complains of nausea and want of appetite.

February 4.—Is again taking nourishment quite freely, and nausea has completely disappeared. She perspires very freely, and feels comfortably warm. The oedema about the eyelids is markedly less, and the patient is passing a larger quantity of urine. She feels her hands smaller, and the veins are once more becoming prominent on the backs of the hands. She does not sleep very well.

February 9.—Her friends notice a marked difference in appearance and speech, which is both stronger and faster. The skin is much softer, the colour better; and the patient feels less unwieldy, and can turn more readily in bed. She complains of aching pains in chest and limbs. The bowels move daily.

February 14.—The patient is 12 lbs. lighter than she was on the 21st January, and there is a great diminution in the oedema, chiefly noticeable in the reduction of the swelling at the back of the neck, and in the reduced size of the legs and hands. The

perspiration is now very free, and is causing desquamation of the skin in large flakes, similar to what occurs in scarlatina. The lips and tongue are smaller, and she is talking with less difficulty, and her spirits are markedly improved. The temperature remains normal.

CASE VI. is that of a man, aged 63, who has been an out-patient at the Royal Public Dispensary during the last six years. He dates the commencement of his symptoms eighteen years back, and had to drop work fifteen years ago, owing to the difficulty he experienced in using his legs and arms. All the usual features of myxœdema were present. He had become much worse during the last two years, and was so weak that he was entirely confined to bed, and was unable to stand unsupported. His speech was so slow and indistinct that it was almost impossible to understand what he was saying. He had delusions of sight and hearing, and was at times delirious. Temperature $95^{\circ}8$ F. Treatment was commenced on the 26th January, $\frac{1}{8}$ th of a thyroid gland being administered twice a week.

February 3.—Not much evidence of improvement in patient's condition. He is still wandering, and seems if anything a little weaker, and great difficulty was experienced in getting him out of bed to have his photograph taken.

February 6.—Patient says that he feels comfortably warm. Temperature has already risen to $97^{\circ}4$. Breath is very offensive, and patient has a decided objection to take any nourishment. Voice seems slightly stronger. The bowels are more regular in their action.

February 11.—Temperature normal. Patient still complains of some amount of nausea, and is restless and sleepless at night. He is perspiring freely.

Dr Church referred to two cases of myxœdema which he had seen. One was in an old gentleman, who died at the age of 60 some years ago. The disease commenced when he was 47. The symptoms of myxœdema were preceded by great depression and suicidal tendencies. Eight years before his death, after taking a Turkish bath, he could not pass his water, and had afterwards to use a catheter daily. His urine became putrid and continued so, and contained a large quantity of mucus. The bladder and prostate were both atrophied. He eventually died with uræmic symptoms and acute bronchitis. The other case was that of a lady 60 years of age. The disease came on six months ago after a fright. He saw her for the first time four months ago. He put her upon thyroid gland, and she had improved very much. As a result of an overdose on one occasion, she suffered from severe prostration; but after forty-eight hours it passed off again. Another unpleasant symptom from which patient had suffered, after this too large dose

of thyroid, was swelling of the parotid and submaxillary glands. Her family history was distinctly phthisical. Seven years ago her son developed exophthalmic goitre. Her sister was similarly affected with myxœdema. Dr Church showed two specimens of dried thyroid, prepared by Duncan, Flockhart, & Co.

Dr George Murray, Newcastle, said there were two common symptoms which had not been referred to. One was the frequent presence of troublesome piles, and the other the occurrence of a thick mucous discharge from the mouth at night. Both of these symptoms disappeared under treatment by thyroid feeding. He explained how he had been led to employ thyroid extract in the treatment of myxœdema. The observations of Kocher upon the effects of thyroidectomy in man, supplemented by the experiments of Victor Horsley upon monkeys, and the discovery by Prof. Schiff that by transplanting thyroid gland into animals the symptoms following thyroidectomy could be prevented, lately put the pathology of myxœdema upon a satisfactory basis. Then Victor Horsley suggested transplantation of thyroid in myxœdema. The improvement that followed this experiment, the result of which was published in August 1890, was immediate; and therefore, he thought, could not be due to the transplanted gland becoming functionally active, as sufficient time had not elapsed for it to become vascularized. This seemed to him strong evidence that the thyroid was a secretory gland. He left the question open as to whether the gland destroyed something harmful to the body or secreted something necessary to keep it in health. He resolved to try the effect of introducing a glycerine extract of the gland into the body in a case of myxœdema. As he thought it probable that the active substance would be destroyed in the stomach, he employed first the hypodermic method. The material he employed consisted of equal parts of thyroid extract, glycerine, and a half per cent. solution of carbolic acid. For administration by the mouth he used the same preparation, without the addition of carbolic acid. One and a half drachm of each preparation was equal to the complete thyroid gland of the sheep. Several other ways of giving the gland had been devised, the latest of which was as a precipitate obtained by treating the glycerine extract with alcohol. In this form it had been given in pills by a doctor in Copenhagen, with marked success. If the hypodermic method was used, he recommended 10 to 15 minims twice a week. If the glycerine extract was given by the mouth, he advised that 10 minims should be administered once or twice a day. It was important to bring on the improvement slowly. He thought it best to take two or three months over the first stage. Over-doses caused rapid pulse, and sometimes palpitation, headache, and vomiting. Undue acceleration of the pulse was to be avoided. It was very important to throw no extra strain upon the heart, especially in old patients, who usually had degenerated arteries and heart. The

patients should be kept very quiet during the first stage. He had lost two cases through not knowing the importance of this. Both had cardiac symptoms before the treatment was started, and died suddenly from syncope through over-exerting themselves when beginning to feel better. Dr Woodhead had observed that several animal extracts caused degeneration of the heart, but he believed that this did not apply to thyroid gland extract. The shortest time in which he had been able to carry out the first stage had been six weeks. The second stage lasted throughout the whole of the patient's life. To maintain health after the first stage had been passed, he recommended 5 to 10 minim doses of the glycerine extract to be given daily by the mouth, or 15 minims once a week hypodermically. He had heard of about 100 cases that had been treated by this method, and, as far as he knew, only three had failed. Two of them, it was probable, had not been correctly treated, as had been pointed out by Dr Lundie. The third was a case recorded in France, which was complicated by exophthalmic goitre. This case was one of special interest, and offered a difficulty to Prof. Greenfield's theory. It was never too late to adopt the treatment. A case of twenty years' standing had been treated very successfully. If treatment was left off for a few weeks, the symptoms returned. On resuming treatment they again disappeared.

Dr Davis, London, said he had had eight cases of myxœdema under his care, seven of which had been treated with thyroid extract. He had latterly used a powdered extract, with very good results. It had been shown that though the gland was given thoroughly cooked it acted equally well.

Dr Stalker, Dundee, said there was a larger proportion of cases of myxœdema in the town from which he came than in any other place he had heard of. He knew of at least twenty-one cases. He had treated three cases by the new method with success. He had found that the parboiled gland acted perfectly well. In reply to a question by the President, he said he did not know if sporadic cretinism was specially prevalent in Dundee.

Dr Foulis said that one of his cases died within twenty-four hours after taking a quarter of a lobe. Profuse diarrhœa set in, and patient became rapidly comatose and died. Another case, which he described, had done very well.

Dr John Thomson gave an account of the post-mortem appearances in a case of myxœdema which died after a few weeks of treatment by thyroid feeding. The following is a full report of the case:—

In December 1887 I showed a case of myxœdema (Annie C.) at a meeting of this Society.¹ I need not now go fully into the facts of her previous history, but I may just mention that she was

¹ *Trans. Edin. Med.-Chir. Soc.*, vol. vii. p. 49.

an unmarried woman, aged 51 years, who presented well-marked but not very severe symptoms of myxedema, and that these had developed very gradually, she having been ill certainly more than ten years. Her case is recorded very fully, along with a most life-like coloured portrait, in Dr Byrom Bramwell's *Atlas of Clinical Medicine*.¹

During the last five years the patient has lived an exceedingly quiet life, and the disease has progressed very slowly. For many months she was greatly relieved by taking 30 minims of tincture of jaborandi three times a day. This kept her skin comfortably moist; but afterwards the dryness of the skin ceased to be a distressing symptom, and she therefore discontinued the medicine. For some years she has had no special treatment for the myxedema. She has continued to suffer constantly from more or less dyspepsia, from constipation and piles, from chilliness, and from a distressing feeling of weakness and disinclination for exertion.

Last August she was very ill with severe pain, which began in the region of the heart and passed down the left arm; it was accompanied by severe dyspeptic symptoms. This recurred frequently for a few weeks, and then passed off; though it returned occasionally afterwards in a less severe form.

On *December 22nd*, 1892, I ordered her to take by the mouth a quarter of a sheep's thyroid twice a week. At this time she had more swelling of the face than she had ever had before, and there were large fatty tumours in both supra-clavicular regions. Her temperature was 97°·5 in the mouth; her pulse 80.

On *December 31st* (after three doses), as she noticed no change in her condition, with the exception of slight headache, she was ordered to take half a thyroid twice a week.

On *January 6th*, the patient complained of severe angina-like pain similar to that which she had had last August. It came on chiefly after exertion, and, starting in the region of the heart, passed down the inner side of the left upper arm, generally stopping abruptly about 2 inches above the elbow, but occasionally felt also over a small area on the dorsum of the hand. On inquiry it was found that she had been exerting herself more than usual, her servant having gone for a holiday. The heart-sounds were weak, but otherwise normal. The swelling of the features was much diminished. Nitro-glycerine (℥j. of a 1 per cent. solution) every four hours was ordered.

On *January 12th*, she was feeling easier. The nitro-glycerine seemed to have relieved the heart-pain considerably; but, as she was very weak, she was told to stay altogether in bed and to stop the thyroid. She had had in all three quarters and three halves of a sheep's thyroid; the last dose having been taken on January 10th.

¹ *Atlas of Clinical Medicine*, vol. i. plate 3.

On *January 17th*, the swelling of her features had almost entirely gone, but she was very weak, and sweating profusely. Her appetite was quite gone, her tongue was thickly furred, and she complained of great nausea and much pain over the stomach. The heart-pain was scarcely felt at all. The temperature in the mouth was $98^{\circ}6$, the pulse 110. Nitro-glycerine stopped.

On *January 23rd*, she got out of bed and nearly fainted. The pain in the stomach was severe, and there was a constant inclination to vomit, but nothing came up. Pulse 108, exceedingly feeble, but quite regular. Hydrochloric acid and pepsin given.

On *January 24th*, as she was no better, she was ordered not to sit up in bed at all, and to take nothing but peptonised milk with whisky every three hours.

On *January 26th*, the pulse and tongue were both better. She was ordered tincture of digitalis, \mathfrak{M} x., thrice daily.

On *January 27th*, Dr Byrom Bramwell kindly saw the patient with me in the afternoon (4.30 P.M.). Her pulse and tongue were both rather more normal, but she did not feel any better.

About 9.30 P.M. she sat up while her bed was being made, and suddenly fainted and died.

A *post-mortem examination* was made, 29th January 1893, at 10.30 A.M., by Dr Byrom Bramwell and myself. Decomposition had already set in to a considerable extent.

Head.—Cerebral arteries atheromatous. Pituitary body enlarged, about the size of a small bean ($1 \times 1\frac{1}{2}$ cms.), and very firm; its fossa unusually deep. Brain otherwise normal.

Thyroid.—Both lobes looked at first sight about normal in outline, but were extremely flabby and thin (like collapsed bladders), so that they could scarcely be felt with the finger among the surrounding tissues even when they had been exposed by dissection.

Thorax.—No remains of thymus. Pleuræ and lungs normal. Pericardium contained about $1\frac{1}{2}$ oz. of blood-stained fluid. Slight thickening of the mitral valve; otherwise all the valves were normal. The muscular tissue of the wall of the heart was in a state of *extreme* degeneration. It was very pale and brownish in colour, and flabby in consistence. In many places it seemed to be largely replaced by fibrous tissue, and in others its place was almost completely taken by fat, owing to advanced atheromatous changes having obstructed the coronary arteries. Numerous soft atheromatous patches in the first part of the aorta.

Abdomen.—Peritoneum normal. Spleen and kidneys seem normal. Liver much decomposed, fatty, with numerous small, rather dry and firm, yellow areas scattered through its substance (? nature). Stomach and bowel not opened; externally they appear normal. Uterus and ovaries practically normal.

Microscopic Report by Dr Gordon Sanders.

The organs, which were markedly decomposed, had been placed in Müller's fluid. After being hardened, they were embedded in paraffin, and stained variously in Ehrlich's hæmatoxylin, hæmatoxylin and eosin, carmine, and the Ehrlich Biondi stain.

Thyroid was greatly altered in aspect. The gland structure was replaced by fibrous tissue: no trace of the glandular elements remaining, except at one or two points where loculi resembling the normal spaces were seen; these, however, contained no epithelium.

The great mass of the tissue was densely fibrous, with few nuclei, but containing bloodvessels of varying sizes, all of whose coats were thickened, especially the middle and outer, which were studded with nuclei. The lumina of the vessels were in some instances filled with blood, in others were much reduced in size by the proliferation of their coats, and were empty.

Scattered throughout the section were seen groups of small cells, staining deeply with hæmatoxylin, with here and there certain large cells, remarkable in their appearance and structure. These cells, which were larger than giant cells, were stained pink with eosin, and contained numerous dark nuclei (or cells?), varying in number from two to six, and having the same shape and size as the small cells forming the clusters above referred to. The outline of these large cells was distinct, but they did not appear to be surrounded by any stroma. Their number in a given cluster was variable, but was on the average about five.

Heart.—Marked increase of the connective tissue throughout the organ; at other parts considerable deposit of fat, especially under the pericardium. The muscular tissue, which was much separated by the connective tissue, was generally atrophied. Under a high power the bundles showed distinct transverse striation; but the nuclei were small, and the whole fibres seemed opalescent. The transverse section showed a remarkable appearance. The centre of the fibre seemed replaced by a yellowish substance, around which the muscular fibre was arranged like the rim of a wheel. The fibre was studded with granules of varying size, some highly refractive. The yellow pigment had no apparent relation to the nucleus.

Skin.—The cutis vera was relatively considerably deeper than the epidermis. The stratum corneum was increased, proliferating and desquamating at parts. The rete malpighii was shallow, consisting of but a few layers of cells which did not stain deeply, except at the basement; otherwise the cells were natural. The upper part of the cutis vera showed a layer of dense connective tissue, but the rest of the true skin seemed more open than usual.

The *hair* structures were altered. The sheaths were increased, and contained numerous deeply-stained nuclei, especially the

outer sheath. The hair itself seemed short and stunted; the papilla seemed normal. The sweat glands and ducts had their connective tissue increased, but the nuclei of the epithelial cells were small and stained poorly. The sebaceous glands did not show any abnormality.

Liver showed chronic venous congestion. The liver cells were cloudy and stained profusely, at parts not taking the stain at all, but remaining a dull brown colour. Otherwise the stroma and vessels and cells showed the usual appearances of the condition.

Kidney also showed chronic venous congestion. The increase in the amount of fibrous tissue was considerable, but the condition of the epithelium precluded an examination of the parenchyma of the organ.

Superior cervical ganglia and *vagus* presented no noteworthy alteration.

Pituitary body (examined by Dr G. Lovell Gulland) was found to be distinctly congested, the capillaries being distended. In some parts of the gland the structure was quite normal, both as to the arrangement of the cells and as to their general character; the chromophile cells were fairly numerous. In other places there was more even than usual of the acinous arrangement, the lumen of the acini being often occupied by colloid material, and the appearance of the sections being very much like that of the thyroid gland at an early stage of development. A certain amount of this cystic formation is normal in the pituitary body, but in this instance there was more of it than usual. The connective tissue of the gland was quite normal.

Remarks.—While the state of the heart muscle which was found in this case was amply sufficient to account for the fatal syncope, one can scarcely doubt, I think, that the thyroid treatment (or, rather, the imperfect application of it) may possibly have had some influence in hastening the end. The dose of the thyroid was certainly small ($2\frac{1}{4}$ thyroids in three weeks), but still it had already demonstrated the activity of its action by the very marked effect it had produced on the subcutaneous swelling.

The lesson which the case teaches is, not that we should refuse to treat patients with unsound hearts, but that our precautions in such cases should be more stringent. The dose should be much smaller than in more robust cases. The patient should be confined to bed from the beginning of the treatment, and means should be taken to insure that directions as to complete rest and the recumbent position are more strictly carried out than they unfortunately were in the case of my patient.

The openers of the discussion having been invited by the President to reply—

Dr Byrom Bramwell said he had nothing to say except to express his admiration and gratitude to *Dr Murray* for this admirable piece of work. They must all recognise the fact that the injection of thyroid extract and thyroid feeding which constituted such a great advance in therapeutics were largely due to *Dr Murray's* initiative.

Prof. Greenfield said he did not like to hear cases spoken of as "cured." He thought it would be of great importance if, in the future, continuous records of the cases were kept for some years, and in the event of any of them dying, if careful post-mortem examinations were made. He advised that, notwithstanding these remarkable results, they should not neglect other remedies as well. Enormous benefit could be gained by the use of hot baths, and by change to a drier and warmer climate. He contended that there was evidence to show that these myxœdematous patients and cretins had far more intelligence than they gave them credit for. How could they explain the total restitution of the mental faculties in a few weeks? The fact was that the patients gave up the attempt to follow conversation and to express their feelings because of their consciousness of the physical difficulties which attended the effort.

Dr Lundie said, with regard to the use of the word "cured," there was no other word in the language that was adequate to express what took place in some of these cases. It was used, as pointed out in his paper, subject to the qualification that the patient had to go on with the treatment throughout life. He thought it was best to employ small and frequent doses, and was glad to hear that *Dr Murray* had come to the same conclusion. They were all certainly immensely indebted to *Dr Murray* for the advance that he had made in the treatment of this disease. They did not know yet what possibilities might be realized as a result of his work. It seemed to open up an immense vista, for there were many other diseases that might be found amenable to similar methods of treatment.

The President said he would like also from the Chair to thank *Dr Murray* for having come there.

Dr Connell, Peebles, moved a vote of thanks to the introducers of the discussion.

Dr Clouston has furnished the following note regarding the mental symptoms in myxœdema, which he was unfortunately prevented from speaking to the Society:—In eight cases of myxœdema it had been attended by mental symptoms of so severe a character that the patients had to be sent to his care in the Asylum, certified as insane. He had never seen any case of the disease where the mental power was not affected more or less. It was, of course, the exception for the mental symptoms to be so marked as to amount to technical insanity, but he thought that it might be assumed as one of the definite symptoms of the disease that all the functions

of the whole brain cortex were altered in some degree. The slowness of voluntary movement, and the great delay in the mental reaction time, were the first mental symptoms. Then came a mental lethargy and hebetude. Along with this there was apt to be an irritability on slight causes, which meant that the mental inhibition was becoming impaired. All through the disease the diminution of control was a very marked symptom. This often led to acts of irrational violence. Then came a general enfeeblement of mental action—a mild dementia. Early in the disease a morbid suspiciousness, that often crystallized into delusions of suspicion, appeared. The intensity and the responsiveness of the affective faculty were found to be lessened. All the mental faculties become in time affected—volition, emotion, power of reasoning, and memory. Yet in no case had he seen complete dementia or acute delirious mania. He had seen suicidal melancholia with attempt at poisoning and refusal of food more than once. In one case the loss of control was shown by dipsomania. The patients were easily affected by domestic annoyance or worry. Most of his asylum patients had sufficiently recovered in mind to leave the asylum and return home after a time, but none of them could be considered satisfactory mental recoveries. It would be one of the most interesting points connected with the thyroid juice treatment to see if that highest and most delicate of all organized structures in nature, the brain cortex, could, after having been in a condition of disturbed nutrition for twenty years, completely recover its sound working. He had two cases now under treatment, one of them of fifteen years' duration, where the mental symptoms were markedly abating. If such a complete cure resulted, it would be one of the most remarkable therapeutic results in the history of medicine. He had found a neurotic heredity to be common, but by no means universal, in the disease. There could be no doubt, however, that myxœdematous insanity—now, he hoped, to disappear for ever, for all the cases would be treated and cured before they reached that stage—might arise without any neurotic heredity, simply from impaired myxœdematous nutrition of the brain cortex. As to the nature of the disease, he was still of the opinion that the nutritional changes could only be explained through the action of the blood deficiency on the trophic centres, and in that sense it might be called, as he long ago called it, a "trophic neurosis," and they would no doubt have to look to the nervous centres for an explanation of the changes in the thyroid.